10/762,730

STN- Structure Search 1.24.05

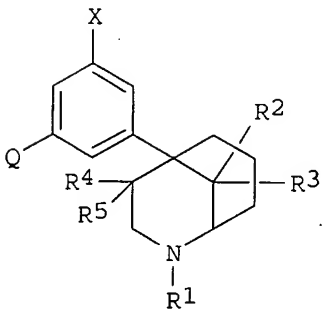
=> d ibib abs hitstr 1-61

L6 ANSWER 1 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:872784 CAPLUS
DOCUMENT NUMBER: 141:366131
TITLE: A preparation of 2-azabicyclo[3.3.1]nonane derivatives useful as opioid receptor antagonists
INVENTOR(S): Coe, Jotham Wadsworth; McHardy, Stanton Furst
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

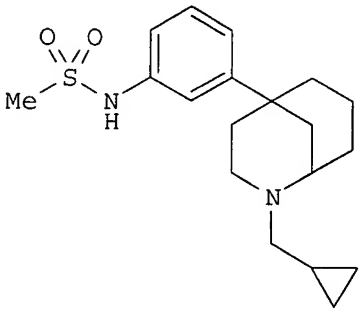
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004089909 | A1 | 20041021 | WO 2004-IB1237 | 20040402 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-462605P P 20030414
OTHER SOURCE(S): MARPAT 141:366131
GI




I

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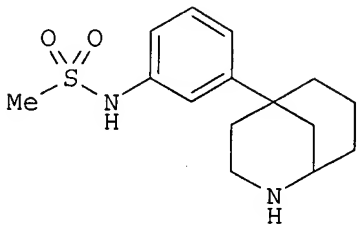
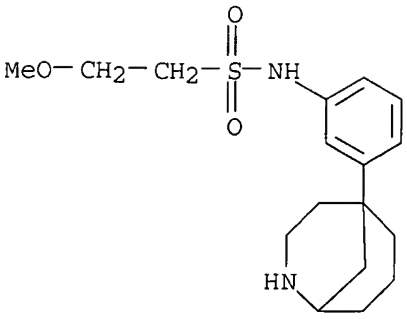
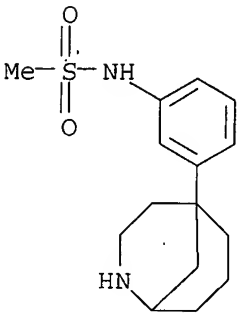



III

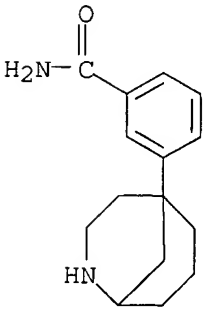
AB The invention relates to a preparation of 2-azabicyclo[3.3.1]nonane derivs. of



RN 777932-73-7 CAPLUS
CN Methanesulfonamide, N-[3-(2-azabicyclo[3.3.1]non-5-yl)phenyl]- (9CI) (CA INDEX NAME)



RN 777932-74-8 CAPLUS
CN Benzamide, .3-(2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

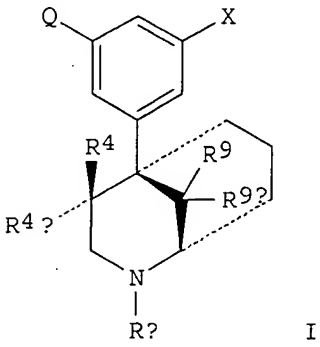
Inventors

L6 ANSWER 2 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:857182 CAPLUS
DOCUMENT NUMBER: 141:350040
TITLE: Preparation of 2-azabicyclo[3.3.1]nonane derivatives as modulators of opioid receptors
INVENTOR(S): Coe, Jotham W.; McHardy, Stanton
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004204445 | A1 | 20041014 | US 2004-762730 | | 20040122 |
| PRIORITY APPLN. INFO.: | | | US 2003-462604P | P | 20030414 |

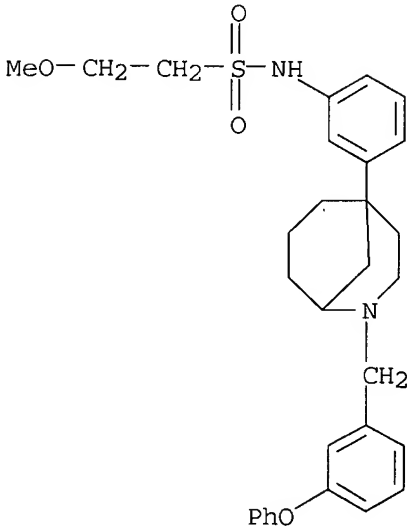
OTHER SOURCE(S): MARPAT 141:350040
GI



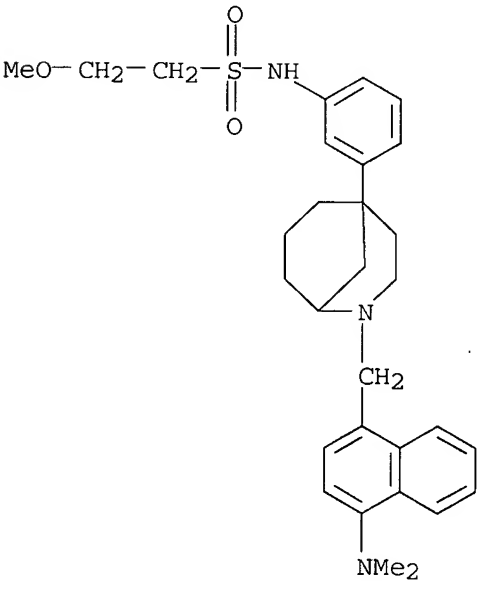
I

AB The title compds. [I; Ra = H, (CH2)nCR1R2R3; X = H, halogen, cyano, -C.tplbond.CR3a, C1-4 alkyl group optionally substituted with from one to three halogen atoms; Q = H, halogen, C1-6 alkyl, cyano, NH2, NH(C1-4 alkyl), N(C1-4 alkyl)2, CONH2, CONH(C1-C4 alkyl), CON(C1-C4 alkyl)2, -NHCHO, NHCOR8, NHSO2R8; R1, R2 = H, , ech (un)substituted C1-6 alkyl, -(CH2)j-aryl, -(CH2)j-heteroaryl (wherein alkyl, aryl, or heteroaryl is optionally substituted); with the carbon to which R1 and R2 are attached, R1 and R2 form an (un)substituted C3-7 carbocyclic or 4- to 7-membered heterocyclic group; R3 is absent or is H, C1-4 alkyl optionally containing one or two unsatd. bonds, OH, C1-4 alkoxy, hydroxy-C1-4 alkyl, (CH2)n-NR10aR10b, -(CH2)n-NHCO(C1-C4 alkyl), -(CH2)n-NO2, -(CH2)n-CN, -(CH2)n-CONH2, (CH2)n-CONH(C1-C4 alkyl), -(CH2)n-CONR10aR10b; R3a = H, C1-6 alkyl optionally substituted with one or more halogen; R4, R4a, R9, R9a = H, C1-4 alkyl, C1-4 alkoxy; R8 = H, C1-6 alkyl, C3-6 cycloalkyl, aryl, -(C2-C4 alkyl)-O-(C1-4 alkyl), aryl, -(CH2)m-NR14R15, 4- to 7-membered heterocyclyl; R10a, R10b, R14, R15 = H, C1-4 alkyl; or R10a and R10b or R14 and R15 connect to form a 4-7 membered heterocyclic ring; R14, R15 = H, C1-C6 alkyl; j, n = independently an integer from 0 to 5] are prepared These compds. bind to and modulate (i.e., inhibit, partially inhibit, activate or partially activate) an opioid receptor or receptors in a mammal, including a human. The subject invention also relates to pharmaceutical compns. comprising such derivs. and methods of using such derivs. to treat disease states, disorders and conditions mediated by opioid receptors, which are selected from the group consisting of irritable bowel syndrome, constipation, nausea, vomiting, pruritic dermatoses, psoriasis, eczema, insect bite, eating disorder, depression, anxiety, schizophrenia, drug addiction, opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's disease, age-related cognitive decline and attention deficit, and hyperactivity disorder. In a μ opioid receptor binding assay to rat forebrain tissue, most of the compds. I, e.g. N-[3-(2-cyclopropylmethyl-2-azabicyclo[3.3.1]non-5-yl)phenyl]methanesulfonamide hydrochloride, tested at 100 nM were found to inhibit [3H]-DAMGO binding at the μu opioid receptor in a range of 10-100%.

azabicyclo[3.3.1]non-5-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 774241-67-7 CAPLUS
CN Ethanesulfonamide, N-[3-[2-[[4-(dimethylamino)-1-naphthalenyl]methyl]-2-azabicyclo[3.3.1]non-5-yl]phenyl]-2-methoxy- (9CI) (CA INDEX NAME)



L6 ANSWER 3 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:633477 CAPLUS
DOCUMENT NUMBER: 141:150963
TITLE: Sigma-2 receptor agonists and their use in the treatment of immunodeficiency virus infection
INVENTOR(S): Crawford, Keith W.; Bowen, Wayne D.; Hildreth, James E.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004064775 | A2 | 20040805 | WO 2004-US739 | 20040114 |

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

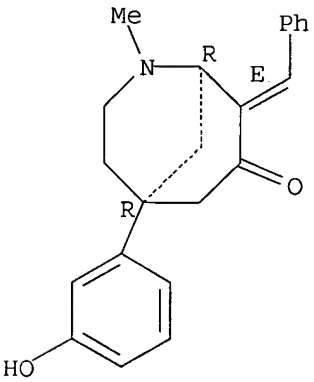
PRIORITY APPLN. INFO.: US 2003-440367P P 20030116

AB The invention discloses sigma-2 receptor agonists and their use in the treatment of immunodeficiency virus infections, especially human immunodeficiency virus (HIV) infections. The invention particularly discloses sigma-2 agonists, especially CB-184 and its analogs, that decrease cellular production of sphingomyelin when provided to recipient cells, and inhibit HIV replication.

IT **157752-20-0**, CB-64D **165307-47-1**, CB-184
**165307-47-1D**, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sigma-2 receptor agonists for treatment of immunodeficiency virus infection)

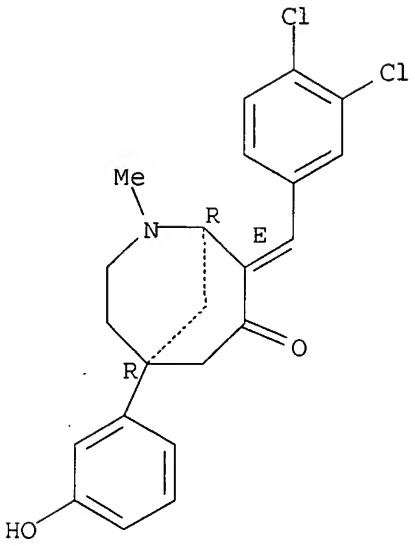
RN 157752-20-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



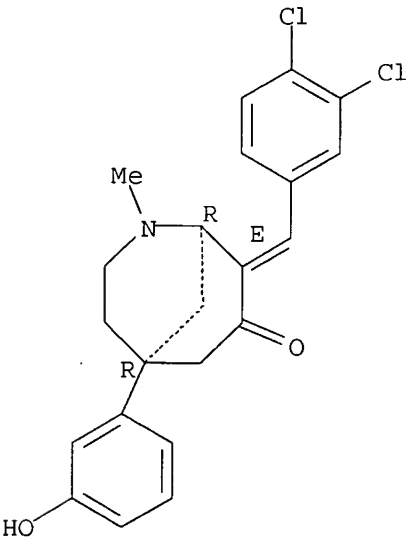

RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



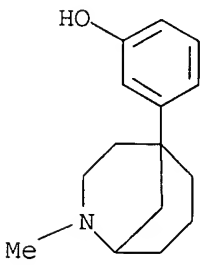

L6 ANSWER 4 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:580825 CAPLUS
DOCUMENT NUMBER: 141:199483
TITLE: A critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans
AUTHOR(S): Kim, In Jong; Dersch, Christina M.; Rothman, Richard B.; Jacobson, Arthur E.; Rice, Kenner C.
CORPORATE SOURCE: Department of Health and Human Services, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0815, USA

SOURCE: Bioorganic & Medicinal Chemistry (2004), 12(16), 4543-4550
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

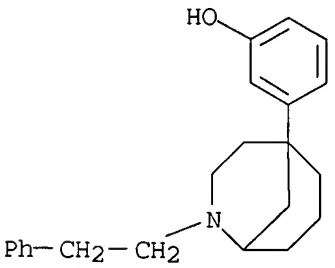
AB The opioid receptor binding affinities of N-methyl- and N-phenethyl-5-phenylmorphans with a meta-hydroxy substituent [3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 3-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] were compared with the affinities of four new ligands bearing an ortho- or para-hydroxyl substituent [2-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol and 2-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol, 4-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenol, and 4-(2-phenethyl-2-azabicyclo[3.3.1]non-5-yl)phenol] that were synthesized from 2-bromoanisole or the known 2-methyl-5-phenyl-2-azabicyclo[3.3.1]nonane, resp. The data indicated that either the electronic state of the phenolic ring is critical for the ligand's interaction with an opioid receptor, or that there must be a specific distance and angle for a hydrogen bond between the phenolic moiety and an amino acid in the binding domain that cannot be altered.

IT **27107-68-2 503156-16-9**
RL: PAC (Pharmacological activity); BIOL (Biological study)
(critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans)

RN 27107-68-2 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

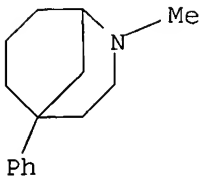



RN 503156-16-9 CAPLUS
CN Phenol, 3-[2-(2-phenylethyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)




IT **744220-55-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(critical structural determinant of opioid receptor interaction with phenolic 5-phenylmorphans)

RN 744220-55-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:565086 CAPLUS
DOCUMENT NUMBER: 141:123632
TITLE: Preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Zhang, Han-zhong; Kuemmerle, Jared D.; Zhang, Hong; Kemnitzer, William E.
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004058253 | A1 | 20040715 | WO 2003-US40308 | 20031218 |
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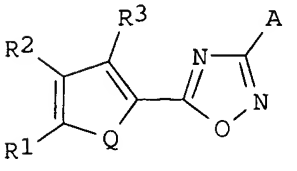
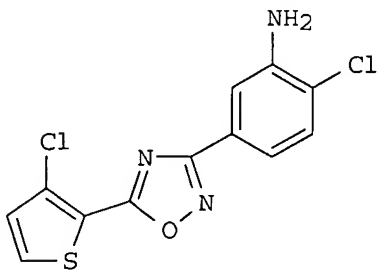
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004127521 | A1 | 20040701 | US 2003-737865 | 20031218 |
| PRIORITY APPLN. INFO.: | | | US 2002-433953P | P 20021218 |

OTHER SOURCE(S): MARPAT 141:123632
GI




I




II

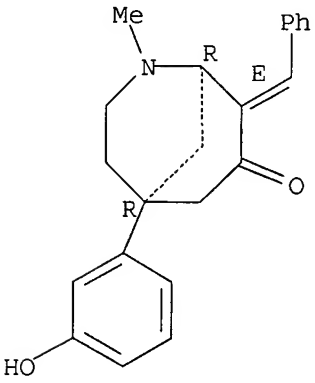
AB Title compds. I [R1-3 = H, halo, haloalkyl, aryl, etc.; Q = S, O, amino; A = heterocycle, carbocycle] are prepared For instance, 3-amino-4-

chlorobenzamidoxime (preparation given) is reacted with 3-chlorothiophene-2-carbonyl chloride (pyridine, reflux, 50 min) to give II. II and other examples are potent caspase cascade activators and inducers of apoptosis in solid tumor cells, e.g., human breast cancer cell lines T-47D and ZR-75-1.

IT **157752-20-0**, CB-64D **165307-47-1**, CB-184
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 3,5-Disubstituted-[1,2,4]-oxadiazoles and analogs as activators of caspases and inducers of apoptosis)

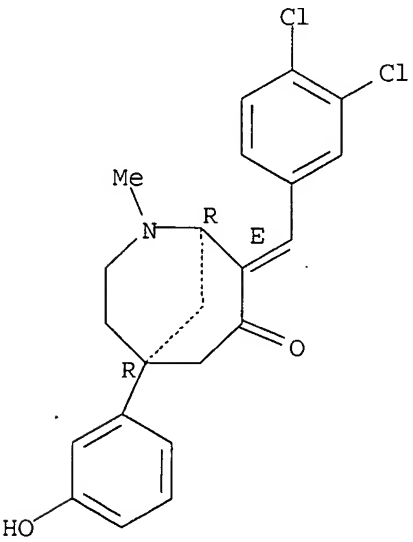
RN 157752-20-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




L6 ANSWER 6 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:534300 CAPLUS
DOCUMENT NUMBER: 141:65094
TITLE: Substituted 1-benzoyl-3-cyano-pyrrolo[1,2-a]quinolines and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Cai, Sui Xiong; Drewe, John A.; Jiang, Sungchun; Kasibhatla, Shailaja; Kuemmerle, Jared Daniel; Sirisoma, Nilantha Sudath; Zhang, Han-Zhong
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

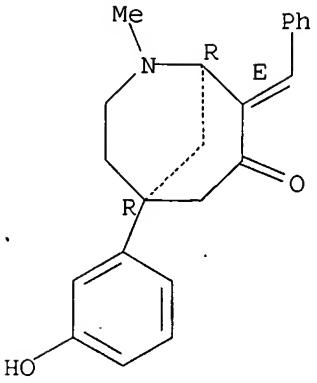
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004055163 | A2 | 20040701 | WO 2003-US39550 | 20031212 |
| WO 2004055163 | A3 | 20040826 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005014759 | A1 | 20050120 | US 2003-733229 | 20031212 |
| PRIORITY APPLN. INFO.: | | | US 2002-432608P P | 20021212 |
| OTHER SOURCE(S): | MARPAT 141:65094 | | | |

AB The invention discloses substituted 1-benzoyl-3-cyanopyrrolo[1,2-a]quinolines and analogs thereof. Compds. of the invention are activators of caspases and inducers of apoptosis. Therefore, the compds. of the invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs. Compound prepn is described.

IT **157752-20-0**, CB-64D **165307-47-1**, CB-184
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(benzoylcyanopyrroloquinolines and analogs as activators of caspases and inducers of apoptosis)

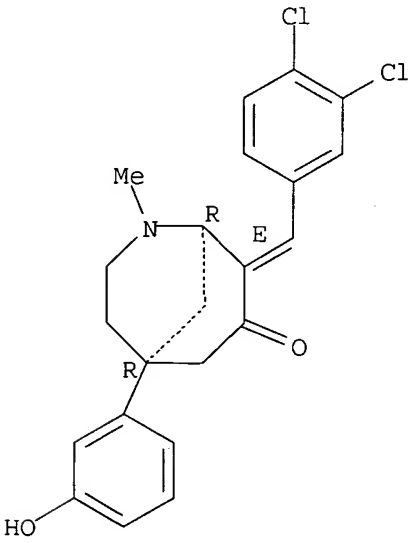
RN 157752-20-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




L6 ANSWER 7 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:489237 CAPLUS |
| DOCUMENT NUMBER: | 141:100133 |
| TITLE: | Sigma-2 receptors are specifically localized to lipid rafts in rat liver membranes |
| AUTHOR(S): | Gebreselassie, Daniel; Bowen, Wayne D. |
| CORPORATE SOURCE: | Unit on Receptor Biochemistry and Pharmacology, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA |
| SOURCE: | European Journal of Pharmacology (2004), 493(1-3), 19-28<br>CODEN: EJPHAZ; ISSN: 0014-2999 |
| PUBLISHER: | Elsevier Science B.V. |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

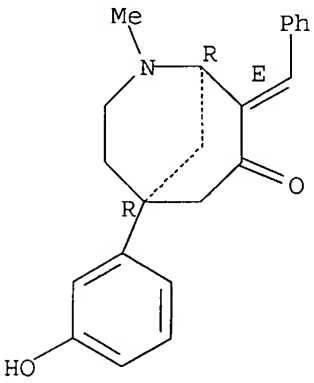
AB The authors have previously shown that sigma-2 receptors are relatively difficult to solubilize. Rat liver membranes were treated on ice with 1% Triton X-100 or 20 mM 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonate (CHAPS), and the extract subjected to centrifugation on a discontinuous gradient of 5%, 38%, and 40% sucrose. Gradient fractions were analyzed for sigma-1 receptors using [3H](+)-pentazocine and for sigma-2 receptors using [3H]1,3-di-o-tolylguanidine ([3H]DTG), in the presence of dextrallorphan. Flotillin-2 was assessed by immunoblotting as a marker for lipid rafts. Sigma-2 receptors were found to discretely co-localize with flotillin-2 in lipid raft fractions. However, sigma-1 receptors were found throughout the gradient. Rafts prepared in CHAPS had sigma-2 receptors with normal pharmacol. characteristics, whereas those in Triton X-100-prepared rafts had about seven-fold lower affinity for [3H]DTG and other ligands. Thus, sigma-2 receptors are resident in membrane lipid rafts, whereas sigma-1 receptors appear in both raft and non-raft membrane domains. Lipid rafts may play an important role in the mechanism of sigma-2 receptor-induced apoptosis.

IT **157752-20-0**, CB64D
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sigma-2 receptors are specifically localized to lipid rafts in rat liver membranes)

RN 157752-20-0 CAPLUS

CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

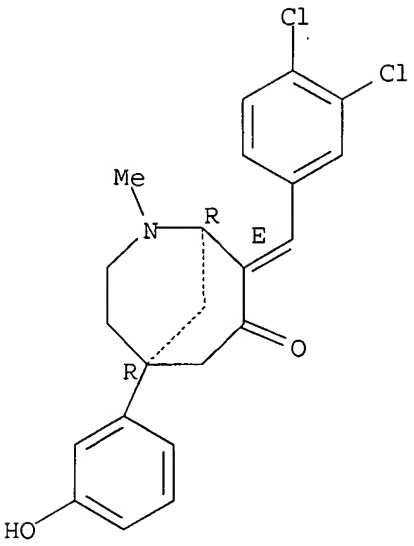
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20448 CAPLUS
DOCUMENT NUMBER: 140:87676
TITLE: Derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis
INVENTOR(S): Tseng, Ben; Sirisoma, Nilantha Sudath; Cai, Sui Xiong; Zhang, Han-Zhong; Kasibhatla, Shailaja; Ollis, Kristin P.; Drewe, John A.
PATENT ASSIGNEE(S): Cytovia, Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:




L6 ANSWER 9 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:965570 CAPLUS
DOCUMENT NUMBER: 140:175001
TITLE: Discovery of the First N-Substituted 4β-Methyl-5-(3-hydroxyphenyl)morphan To Possess Highly Potent and Selective Opioid δ Receptor Antagonist Activity
AUTHOR(S): Carroll, F. Ivy; Zhang, Li; Mascarella, S. Wayne; Navarro, Hernan A.; Rothman, Richard B.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Thomas, James B.
CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(2), 281-284
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A structurally novel opioid δ receptor selective antagonist has been identified. This compound, (+)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-7-yl-(1-phenyl-1-cyclopentane)carboxamide [(+)-KF4], showed a Ke value of 0.15 nM in the [35S]GTPγS functional assay. (+)-KF4 is also a δ inverse agonist with an IC50 value of 1.8 nM. To the authors knowledge, this is the first potent and selective δ opioid receptor antagonist from the 5-phenylmorphan class of opioids.

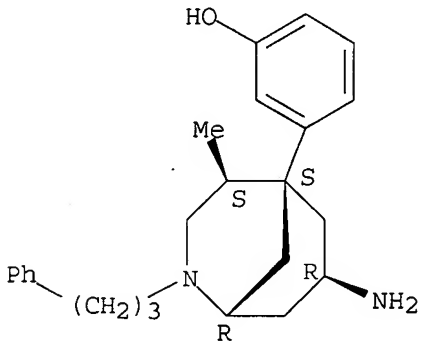
IT **658713-91-8P 658713-92-9P 658713-93-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(discovery of first N-substituted methyl(3-hydroxyphenyl)morphan to possess highly potent and selective opioid δ receptor antagonist activity and inverse agonist activity)

RN 658713-91-8 CAPLUS
CN Cyclopentanecarboxamide, N-[(1R,4R,5S,6R)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-6-yl]-1-phenyl- (9CI) (CA INDEX NAME)

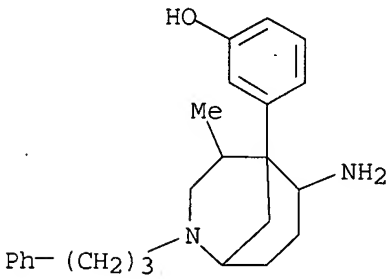
Absolute stereochemistry. Rotation (+).

CN Phenol, 3-[(1R,4S,5S,7R)-7-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

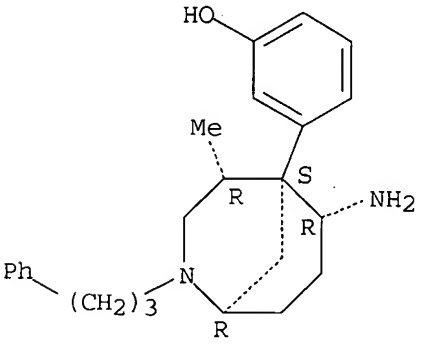



RN 658713-94-1 CAPLUS
CN Phenol, 3-[6-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)




RN 658713-95-2 CAPLUS
CN Phenol, 3-[(1R,4R,5S,6R)-6-amino-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:443323 CAPLUS
DOCUMENT NUMBER: 139:246129

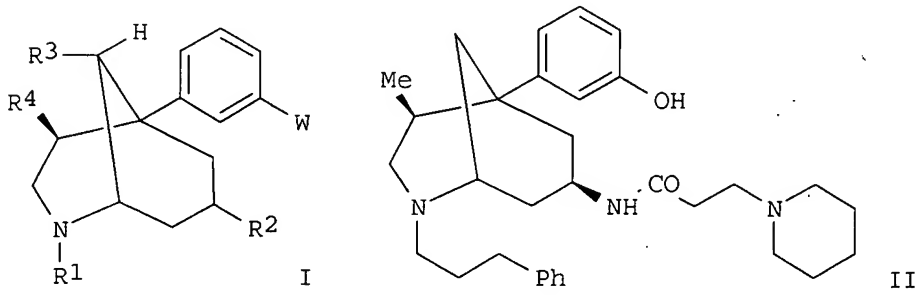
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:594678 CAPLUS
DOCUMENT NUMBER: 137:155089
TITLE: Preparation of azabicyclononanes for therapeutic use as κ opioid receptor ligands for the treatment of cocaine or heroin addiction
INVENTOR(S): Carroll, F. Ivy; Thomas, James B.; Mascarella, S. Wayne
PATENT ASSIGNEE(S): Research Triangle Institute, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

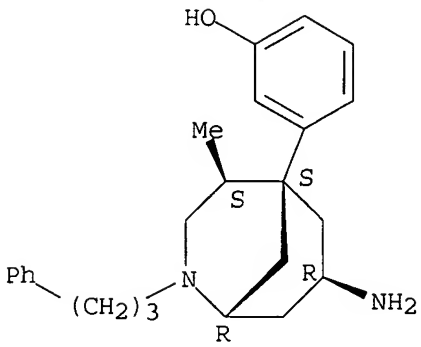
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002060445 | A1 | 20020808 | WO 2002-US1231 | 20020201 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002143145 | A1 | 20021003 | US 2001-774566 | 20010201 |
| US 6559159 | B2 | 20030506 | | |
| CA 2436409 | AA | 20020808 | CA 2002-2436409 | 20020201 |
| EP 1363629 | A1 | 20031126 | EP 2002-704144 | 20020201 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004520383 | T2 | 20040708 | JP 2002-560637 | 20020201 |

PRIORITY APPLN. INFO.: US 2001-774566 A 20010201
WO 2002-US1231 W 20020201

OTHER SOURCE(S): MARPAT 137:155089
GI

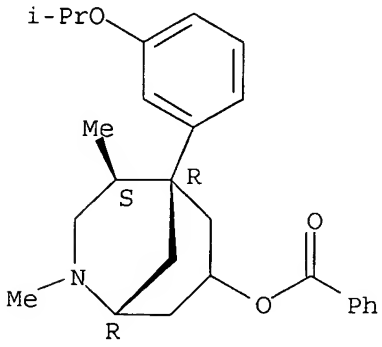



AB Structurally novel κ opioid receptor antagonists, such as I [R1 = alkyl, alkenyl, alkynyl, arylalkyl, etc; R2 = acylamino, carbamoyl, carboxyl, aminoalkyl, heterocyclylalkyl, etc.; R3 = H, alkyl, alkenyl, alkynyl, arylalkyl, carboxyl; R4 = H, alkyl, alkenyl, alkynyl, arylalkyl;



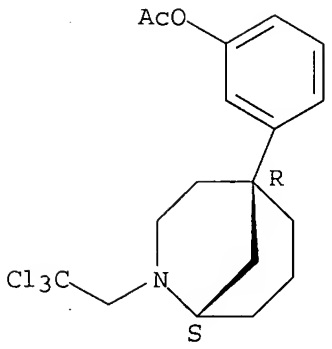

RN 444904-25-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-ol, 2,4-dimethyl-5-[3-(1-methylethoxy)phenyl]-, benzoate (ester), (1R,4S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



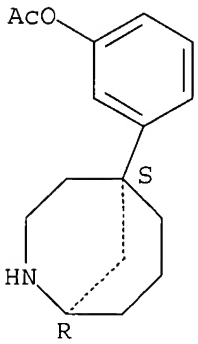

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:583529 CAPLUS
DOCUMENT NUMBER: 138:265113
TITLE: Probes for Narcotic Receptor Mediated Phenomena. Part 28: New Opioid Antagonists from Enantiomeric Analogues of 5-(3-Hydroxyphenyl)-N-phenylethylmorphan
AUTHOR(S): Hashimoto, Akihiro; Jacobson, Arthur E.; Rothman, Richard B.; Dersch, Christina M.; George, Clifford; Flippen-Anderson, Judith L.; Rice, Kenner C.
CORPORATE SOURCE: National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Medicinal Chemistry, National Institutes of Health, Bethesda, MD, 20892-0815, USA
SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(10), 3319-3329
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:265113
AB Enantiomeric analogs of 5-(3-hydroxyphenyl)morphan ligands were synthesized and evaluated because of our unexpected finding that opioid antagonists can be obtained in the 5-phenylmorphan series of opioids without sterically hindering the rotation of the phenolic ring. We determined the opioid receptor binding affinity of these new analogs, as well as the



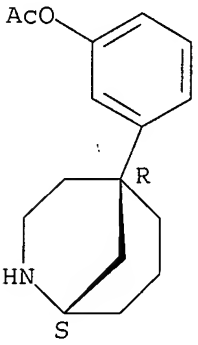

RN 503156-10-3 CAPLUS
CN Phenol, 3-(1R,5S)-2-azabicyclo[3.3.1]non-5-yl-, acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 503156-11-4 CAPLUS
CN Phenol, 3-(1S,5R)-2-azabicyclo[3.3.1]non-5-yl-, acetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:509530 CAPLUS
DOCUMENT NUMBER: 137:216844
TITLE: Discovery of an Opioid κ Receptor Selective Pure

Antagonist from a Library of N-Substituted 4β-Methyl-5-(3-hydroxyphenyl)morphans

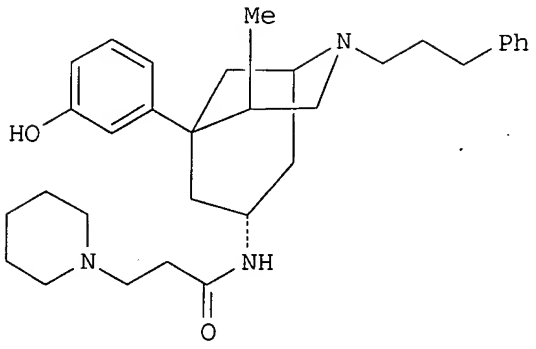
AUTHOR(S): Thomas, James B.; Atkinson, Robert N.; Namdev, Nivedita; Rothman, Richard B.; Gigstad, Kenneth M.; Fix, Scott E.; Mascarella, S. Wayne; Burgess, Jason P.; Vinson, N. Ariane; Xu, Heng; Dersch, Christina M.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy

CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Medicinal Chemistry (2002), 45(16), 3524-3530
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:216844

GI




I

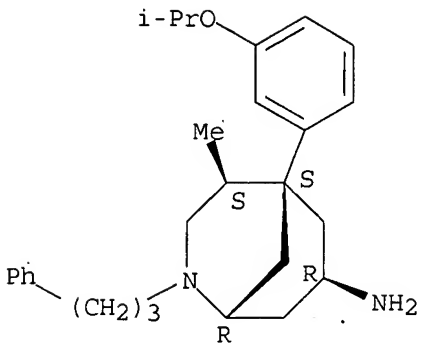
AB A library of compds. biased toward opioid receptor antagonist activity was prepared by incorporating N-phenylpropyl-4β-methyl-5-(3-hydroxyphenyl)morphans as the core scaffold using simultaneous solution phase synthetic methodol. From this library, N-phenylpropyl-4β-methyl-5-(3-hydroxyphenyl)-7α-[3-(1-piperidinyl)propanamido]morphan (I) was identified as the first potent and selective κ opioid receptor antagonist from the 5-phenylmorphan class of opioids.

IT **455311-44-1P 455311-45-2P 455311-46-3P**
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation)
(discovery of an opioid κ receptor selective pure antagonist from a library of N-substituted 4β-methyl-5-(3-hydroxyphenyl)morphans)

RN 455311-44-1 CAPLUS

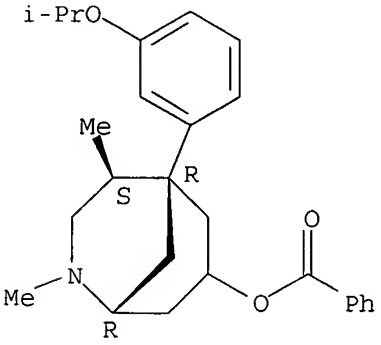
CN Butanamide, 4-(dimethylamino)-N-[(1S,4R,5R,7S)-5-(3-hydroxyphenyl)-4-methyl-2-(3-phenylpropyl)-2-azabicyclo[3.3.1]non-7-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




RN 444904-25-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-ol, 2,4-dimethyl-5-[3-(1-methylethoxy)phenyl]-, benzoate (ester), (1R,4S,5R)- (9CI) (CA INDEX NAME)

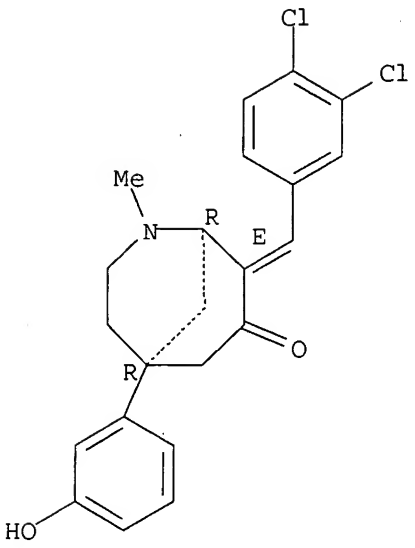
Absolute stereochemistry.




REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:70938 CAPLUS
DOCUMENT NUMBER: 136:363394
TITLE: Sigma-2 receptor agonists activate a novel apoptotic pathway and potentiate antineoplastic drugs in breast tumor cell lines
AUTHOR(S): Crawford, Keith W.; Bowen, Wayne D.
CORPORATE SOURCE: Department of Pharmacology, Howard University College of Medicine, Washington, DC, 20059, USA
SOURCE: Cancer Research (2002), 62(1), 313-322
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have reported previously that sigma-2 receptors are expressed in high densities in a variety of tumor cell types and that various sigma ligands have cytotoxic effects. Other investigators have demonstrated increased expression of sigma-2 receptors in rapidly proliferating tumors and the ability of some sigma ligands to inhibit proliferation. We demonstrate here the ability of sigma-2 receptor agonists to induce cell death by a mechanism consistent with apoptosis. In breast tumor cell lines that are sensitive (MCF-7) and resistant (MCF-7/Adr-, T47D, and SKBr3) to antineoplastic agents, incubation with the sigma-2 subtype-selective agonists CB-64D and CB-184 produced dose-dependent cytotoxicity (measured by lactate dehydrogenase release into medium). The EC50 for this response




REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:833074 CAPLUS
DOCUMENT NUMBER: 135:366722
TITLE: Potentiation of antineoplastic agents using sigma-2 ligands
INVENTOR(S): Crawford, Keith W.; Bowen, Wayne D.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001085153 | A2 | 20011115 | WO 2001-US40688 | 20010508 |
| WO 2001085153 | A3 | 20020815 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001063502 | A5 | 20011120 | AU 2001-63502 | 20010508 |
| US 2003171397 | A1 | 20030911 | US 2003-275830 | 20030509 |
| PRIORITY APPLN. INFO.: | | | US 2000-203220P P | 20000511 |
| | | | WO 2001-US40688 W | 20010508 |

OTHER SOURCE(S): MARPAT 135:366722

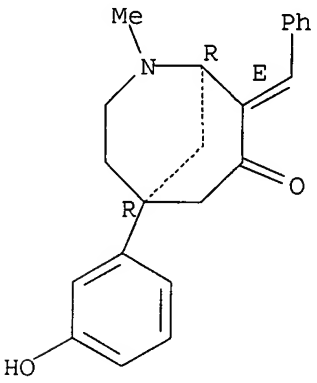
AB The invention discloses the use of sigma-2 agonists to potentiate the activity of antineoplastic agents. These substances are useful for treating cancerous tumors and, in particular, drug-resistant tumors in humans. Methods for sensitizing multidrug resistant cells to antitumor agents comprising contacting the cells with a sigma-2 agonist are also

described.

IT **157752-20-0**, CB 64D **165307-47-1**, CB 184
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sigma-2 agonist for antineoplastic agent potentiation)

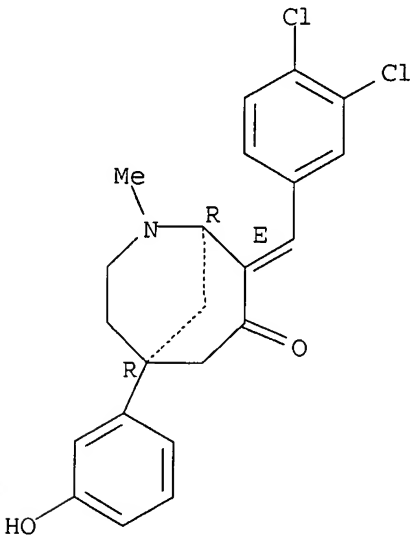
RN 157752-20-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




L6 ANSWER 16 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:892230 CAPLUS
DOCUMENT NUMBER: 134:231497
TITLE: Opioid peptide receptor studies. 14. Stereochemistry determines agonist efficacy and intrinsic efficacy in

the [35S]GTP-γ-S functional binding assay

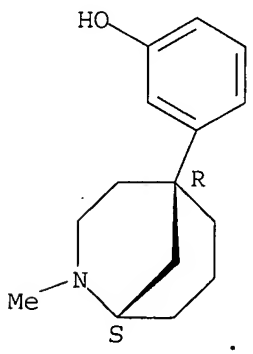
AUTHOR(S): Xu, Heng; Hashimoto, Akihiro; Rice, Kenner C.; Jacobson, Arthur E.; Thomas, James B.; Carroll, F. Ivy; Lai, Josephine; Rothman, Richard B.
CORPORATE SOURCE: CPS, DIR, NIDA, Baltimore, MD, 21224, USA
SOURCE: Synapse (New York) (2001), 39(1), 64-69
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous data obtained with the cloned rat μ opioid receptor demonstrated that stereochem. affects the four parameters of the ligand-receptor interaction: potency (ED50), efficacy (maximal stimulation), intrinsic efficacy (effect as a function of receptor occupation), and binding affinity. This study evaluated the activities of structurally diverse opioid receptor ligands in the [35S]GTP-γ-S binding assay, comparing the relationship between receptor binding, activation, efficacy, and intrinsic efficacy. The data, obtained with cloned rat μ receptors, demonstrated that an analgetic, (-)-5-m-hydroxyphenyl-2-methylmorphan (NIH8508), and its (+)-isomer (NIH8509), behave as partial agonists, but had different intrinsic efficacy in the [35S]GTP-γ-S binding assay. Replacement of the Me group with the phenethyl group on the piperidine nitrogen of NIH8508 and NIH8509 [(1R,5S)-AH019 and (1S,5R)-AH019] increased affinity for the μ receptor and eliminated any agonist effect, supporting the hypothesis that certain structural features make these compds. antagonists. These study also show that all of the fully efficacious μ agonists studied here had high levels of intrinsic efficacy, producing a 50% response at about 10% receptor occupancy. Comparison of the binding Ki in competitively inhibiting [125I]OXY binding to the functional Ki for opioid antagonists [Ki(IOXY)/Ki(GTP-γ-S)] provides more detailed evidence that the [35S]GTP-γ-S binding assay can be used to reliably determine apparent functional antagonist Ki values in addition to agonist ED50, efficacy and intrinsic efficacy.

IT **28623-81-6**, NIH 8509 **28623-84-9**, NIH 8508
**330625-46-2**, (1R,5S)-AH 019 **330625-47-3**, (1S,5R)-AH 019
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(opioid peptide receptor studies. 14. stereochem. dets. agonist efficacy and intrinsic efficacy in the [35S]GTP-γ-S functional binding assay)

RN 28623-81-6 CAPLUS
CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).




RN 28623-84-9 CAPLUS

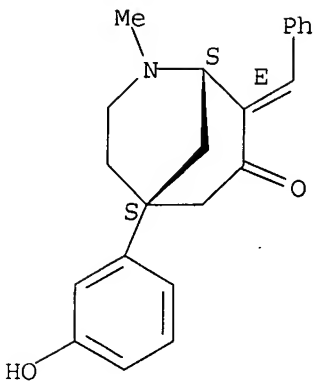
L6 ANSWER 17 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:171768 CAPLUS
DOCUMENT NUMBER: 132:318283
TITLE: Modulation of cellular calcium by sigma-2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells
AUTHOR(S): Vilner, Bertold J.; Bowen, Wayne D.
CORPORATE SOURCE: Unit on Receptor Biochemistry and Pharmacology, Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 292(3), 900-911
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human SK-N-SH neuroblastoma cells expressed sigma-1 and sigma-2 receptors with similar pharmacol. profiles to those of rodent-derived tissues, although sigma-2 receptors exhibited some affinity differences that might suggest heterogeneity or species differences. Structurally diverse sigma ligands produced two types of increases in intracellular (cytosolic) Ca2+ concentration ([Ca2+]i) in these cells. CB-64D, CB-64L, JL-II-147, BD737, LR172, BD1008, haloperidol, reduced haloperidol, and ibogaine all produced an immediate, dose-dependent, and transient rise in [Ca2+]i. Sigma-inactive compds. structurally similar to the most active sigma ligands and ligands for several neurotransmitter receptors produced little or no effect. The high activity of CB-64D and ibogaine (sigma-2-selective ligands) compared with the low activity of (+)-pentazocine and other (+)-benzomorphans (sigma-1-selective ligands), in addition to enantioselectivity for CB-64D over CB-64L, strongly indicated mediation by sigma-2 receptors. The effect of CB-64D and BD737 was blocked by the sigma antagonists BD1047 and BD1063, further confirming specificity as a receptor-mediated event. The transient rise in [Ca2+]i occurred in the absence of extracellular Ca2+ and was completely eliminated by pretreatment of cells with thapsigargin. Thus, sigma-2 receptors stimulate a transient release of Ca2+ from the endoplasmic reticulum. Prolonged exposure of cells to sigma-receptor ligands resulted in a latent and sustained rise in [Ca2+]i, with a pharmacol. profile identical to that of the transient rise. This sustained rise in [Ca2+]i was affected by neither the removal of extracellular Ca2+ nor thapsigargin pretreatment, suggesting latent sigma-2 receptor-induced release from thapsigargin-insensitive intracellular Ca2+ stores. Sigma-2 receptors may use Ca2+ signals in producing cellular effects.

IT **157752-18-6**, CB 64L **266691-71-8**, CB 53D
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(modulation of cellular calcium by σ-2 receptors: release from intracellular stores in human SK-N-SH neuroblastoma cells)

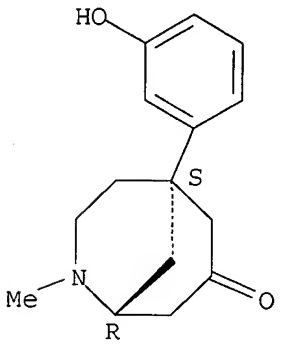
RN 157752-18-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1S,5S,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.




RN 266691-71-8 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-, (1R,5S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L6 ANSWER 18 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:594935 CAPLUS
DOCUMENT NUMBER: 131:228652
TITLE: Preparation of substituted piperidines for pharmaceutical use as opioid antagonists
INVENTOR(S): Carroll, Frank Ivy
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9945925 | A1 | 19990916 | WO 1999-US5131 | 19990309 |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,

| | | | | | |
|---|---|---|---|---|---|
| | CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2324418 | | AA | 19990916 | CA 1999-2324418 | 19990309 |
| AU 9930738 | | A1 | 19990927 | AU 1999-30738 | 19990309 |
| AU 756983 | | B2 | 20030130 | | |
| EP 1061919 | | A1 | 20001227 | EP 1999-912345 | 19990309 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002506032 | | T2 | 20020226 | JP 2000-535340 | 19990309 |
| US 2002165396 | | A1 | 20021107 | US 2002-100097 | 20020319 |
| US 6552032 | | B2 | 20030422 | | |
| US 2002169324 | | A1 | 20021114 | US 2002-100096 | 20020319 |
| US 6593348 | | B2 | 20030715 | | |
| US 2002193602 | | A1 | 20021219 | US 2002-99948 | 20020319 |
| US 6531481 | | B2 | 20030311 | | |
| US 2003158415 | | A1 | 20030821 | US 2002-266774 | 20021009 |
| US 2004146518 | | A1 | 20040729 | US 2003-742782 | 20031223 |
| PRIORITY APPLN. INFO.: | | | | US 1998-77402P | P 19980310 |
| | | | | US 1998-107902P | P 19981110 |
| | | | | WO 1999-US5131 | W 19990309 |
| | | | | US 2000-623872 | A3 20001127 |
| | | | | US 2002-99948 | A1 20020319 |

OTHER SOURCE(S): MARPAT 131:228652
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

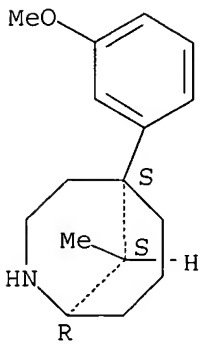
AB Piperidine containing heterocyclic compds. I [R1, R2 = H, alkyl, aryl, arylalkyl; R3 = alkyl, cycloalkyl, aryl, arylalkyl, etc.], II [R1 = alkyl, arylalkyl; R3, R4, R5, R6 = H, OH, NH2, CN, CF3, CN, NO2, alkyl, alkyloxy, halogen, amino, etc.; R7 = H, alkyl], and III [R1 = alkyl, arylalkyl; R2 = H, NH2, :O, alkyl, arylalkyl, amino, etc.] were prepared for use as opioid antagonists to treat a variety of disease states which involve the opioid receptors. Thus, the hydrochloride salt of piperidine IV [R3 = (CH2)2C6H4-4-OH], i.e. RTI 5989-29, was prepared starting from (+)-(3R,4R)-dimethyl-4-(3-hydroxyphenyl)piperidine, N-(tert-butoxycarbonyl)-L-valine, and 3-(4-hydroxyphenyl)propanoic acid. The prepared heterocyclic compds. containing a piperidine subunit were tested for κ-, μ-, and δ-opioid receptor binding activity.

IT **244048-54-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. containing a piperidine subunit for pharmaceutical use as opioid antagonists)

RN 244048-54-2 CAPLUS

CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

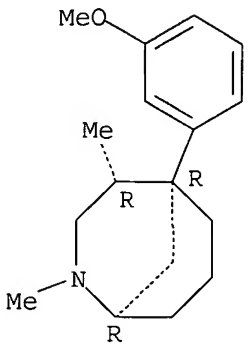
L6 ANSWER 19 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:98322 CAPLUS
DOCUMENT NUMBER: 130:182632
TITLE: A stereoselective synthetic approach to N-alkyl-4β-methyl-5-phenylmorphans
AUTHOR(S): Thomas, James B.; Gigstad, Kenneth M.; Fix, Scott E.; Burgess, Jason P.; Cooper, Julie B.; Mascarella, S. Wayne; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
SOURCE: Tetrahedron Letters (1999), 40(3), 403-406
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:182632

AB A convergent, highly stereoselective synthetic approach to N-alkyl-4β-methyl-5-phenylmorphans has been developed utilizing alkylation of the metalloenamine of N-alkyl-1,2,3,6-tetrahydro-4-phenylpyridines with 2-(chloromethyl)-3,5-dioxahex-1-ene (Okahara's reagent) followed by Clemmensen reduction

IT **220503-24-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(a stereoselective synthetic approach to N-alkyl-4β-methyl-5-phenylmorphans)

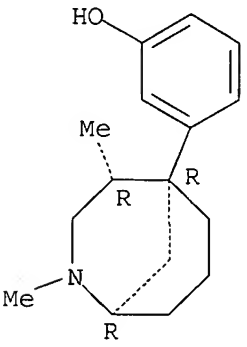
RN 220503-24-2 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2,4-dimethyl-, (1R,4R,5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



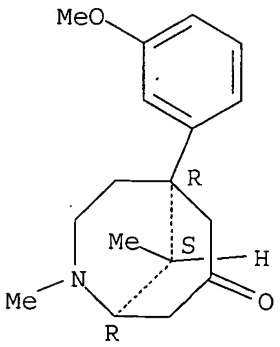

IT **220503-21-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(a stereoselective synthetic approach to N-alkyl-4β-methyl-5-phenylmorphans)
RN 220503-21-9 CAPLUS
CN Phenol, 3-[(1R,4R,5R)-2,4-dimethyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:603858 CAPLUS
DOCUMENT NUMBER: 129:316409
TITLE: Synthesis of 9β-methyl-2-alkyl-7-oxo-5-arylmorphans
AUTHOR(S): Thomas, James B.; Zheng, Xiaoling; Brieaddy, Lawrence E.; Burgess, Jason P.; Mascarella, S. Wayne; Fix, Scott E.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
CORPORATE SOURCE: Chem. Life Sci., Res. Triangle Inst., Research Triangle Park, NC, 27709, USA
SOURCE: Tetrahedron Letters (1998), 39(39), 7001-7004
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:316409
AB A convergent synthetic approach to 9β-methyl-2-alkyl-7-oxo-5-arylmorphans has been developed utilizing alkylation of the metalloenamine of 1,2,3,6-tetrahydro-4-aryl-1-alkylpyridines with 2-(chloromethyl)-3,5-



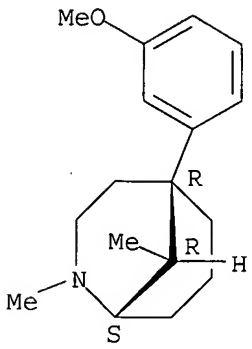

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:600696 CAPLUS
DOCUMENT NUMBER: 129:325731
TITLE: N-Substituted 9β-Methyl-5-(3-hydroxyphenyl)morphans Are Opioid Receptor Pure Antagonists
AUTHOR(S): Thomas, James B.; Zheng, Xiaoling; Mascarella, S. Wayne; Rothman, Richard B.; Dersch, Christina M.; Partilla, John S.; Flippen-Anderson, Judith L.; George, Clifford F.; Cantrell, Buddy E.; Zimmerman, Dennis M.; Carroll, F. Ivy
CORPORATE SOURCE: Chemistry and Life Sciences, Research Triangle Institute, Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(21), 4143-4149
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibition of radioligand binding and [35S]GTPγS functional assay data for N-methyl- and N-phenethyl-9β-methyl-5-(3-hydroxyphenyl)morphans (I and II) show that these compds. are pure antagonists at the μ, δ, and κ opioid receptors. Since I and II have the 5-(3-hydroxyphenyl) group locked in a conformation comparable to an equatorial group of a piperidine chair conformation, this information provides very strong evidence that opioid antagonists can interact with opioid receptors in this conformation. In addition, it suggests that the trans-3,4-dimethyl-4-(3-hydroxyphenyl)piperidine class of antagonist operates via a Ph equatorial piperidine chair conformation. Importantly, the close relationship between the 4-(3-hydroxyphenyl)piperidines and 5-(3-hydroxyphenyl)morphan antagonists shows that the latter class of compound provides a rigid platform on which to build a novel series of opioid antagonists.

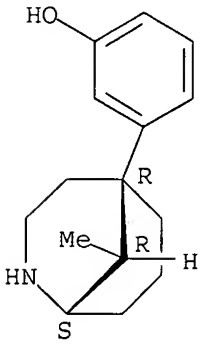
IT **215124-71-3P 215124-72-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and opioid receptor antagonist activity of N-substituted 9β-methyl-5-(3-hydroxyphenyl)morphans)

RN 215124-71-3 CAPLUS
CN Phenol, 3-[(1R,5S,9S)-2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl]-, hydrochloride, rel- (9CI) (CA INDEX NAME)




RN 215124-76-8 CAPLUS
CN Phenol, 3-[(1R,5S,9S)-9-methyl-2-azabicyclo[3.3.1]non-5-yl]-, rel- (9CI) (CA INDEX NAME)

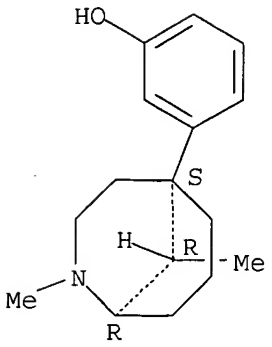
Relative stereochemistry.




REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 22 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:482972 CAPLUS
DOCUMENT NUMBER: 125:185593
TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1995)
AUTHOR(S): Aceto, M. D.; Bowman, E. R.; Harris, L. S.; May, E. L.
CORPORATE SOURCE: Medical College Virginia, Virginia Commonwealth University, Richmond, VA, USA
SOURCE: NIDA Research Monograph (1996), 162(Problems of Drug Dependence, 1995), 408-451
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of a series of drugs to produce dependence was studied in rhesus monkeys, rats, and mice.
IT **88550-29-2**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(dependence studies of new compds. in rhesus monkey and rat and mouse)
RN 88550-29-2 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



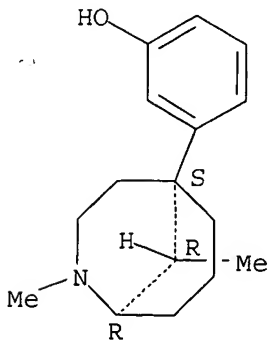
L6 ANSWER 23 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:482970 CAPLUS
DOCUMENT NUMBER: 125:185591
TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. XIX. Drug evaluation committee of the College on Problems of Drug Dependence, Inc. (1995)
AUTHOR(S): Jacobson, A. E.
CORPORATE SOURCE: Labortory Medicinal Chemistry, National Institute Diabetes Digestive Kidney Diseases, Bethesda, MD, USA
SOURCE: NIDA Research Monograph (1996), 162(Problems of Drug Dependence, 1995), 363-376
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The phys. dependence potential and abuse liability of various analgesics and stimulants and depressants is described and related to their biol. activities.

IT **88550-29-2**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. evaluation of compds. for phys. dependence potential and abuse liability of analgesics and stimulants and depressants)

RN 88550-29-2 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.

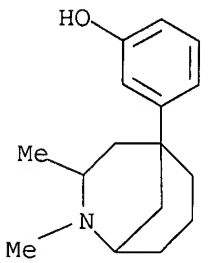


L6 ANSWER 24 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:350730 CAPLUS
DOCUMENT NUMBER: 125:132417
TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. XVII. Drug Evaluation Committee of the College on Problems of Drug Dependence, Inc. (1993)
AUTHOR(S): Jacobson, A. E.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1994), 140(Problems of Drug Dependence 1993, Vol. 1), 179-195
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Drug Evaluation Committee (DEC) of the CPDD (Dr. T. Cicero, Chairman) is charged with the responsibility of determining the phys. dependence potential and abuse liability of potential analgesics, stimulants, and depressants, and with associated methodol. research. The drugs are obtained from investigators in universities, industrial groups, and the public sector. The testing function is carried out under the auspices of the CPDD as a public service and has provided information to pharmaceutical industry and governmental agencies for the appropriate scheduling of a drug with the potential for abuse. The information which DEC provides to university researchers, who frequently work under a NIDA grant, is useful for determining the desirability of structural modification of a drug and the DEC biol. data are often needed for publication of their work in medicinal chemical journals. Data are reported for 61 compds.

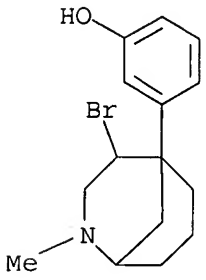
IT **178896-97-4**, NIH 10779 **178935-97-2**, NIH 10778
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. evaluation of drugs for their phys. dependence potential and abuse liability)

RN 178896-97-4 CAPLUS
CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI) (CA INDEX NAME)




● HCl

RN 178935-97-2 CAPLUS
CN Phenol, 3-(4-bromo-2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)

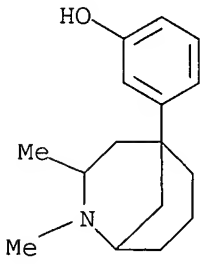



L6 ANSWER 25 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:343479 CAPLUS
DOCUMENT NUMBER: 125:104826
TITLE: Dependence studies of new compounds in the rhesus monkey, rat and mouse (1994)
AUTHOR(S): Aceto, M.D.; Bowman, E.R.; Harris, L.S.; May, E.L.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1995), 152(Problems of Drug Dependence 1994, Vol. 1), 162-212
CODEN: MIDAD4; ISSN: 0361-8595
PUBLISHER: National Institute on Drug Abuse
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twenty-eight compds. were examined in rhesus monkey, rat, and mouse for antinociceptive activity, ability to substitute for morphine, and development of phys. dependence. The data acquired were compared with several standard drugs.

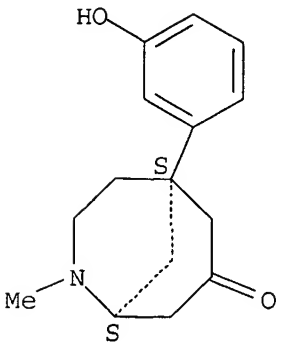
IT **178896-97-4**, NIH 10779
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dependence studies of new compds. in the rhesus monkey, rat and mouse)

RN 178896-97-4 CAPLUS
CN Phenol, 3-(2,3-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride (9CI) (CA INDEX NAME)

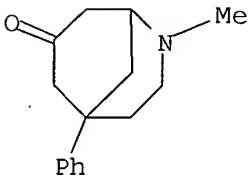



● HCl

L6 ANSWER 26 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:241972 CAPLUS
DOCUMENT NUMBER: 124:343158
TITLE: Probes for Narcotic Receptor-Mediated Phenomena. 21. Novel Derivatives of 3-(1,2,3,4,5,11-Hexahydro-3-

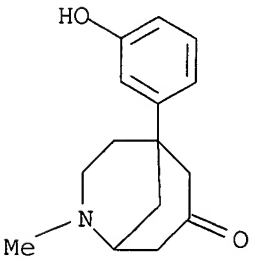


RN 176699-46-0 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 176699-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-, hydrobromide (9CI) (CA INDEX NAME)



● HBr

L6 ANSWER 27 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:905946 CAPLUS
DOCUMENT NUMBER: 123:305990
TITLE: (E)-8-Benzylidene Derivatives of 2-Methyl-5-(3-hydroxyphenyl)morphans: Highly Selective Ligands for the σ2 Receptor Subtype
AUTHOR(S): Bertha, Craig M.; Vilner, Bertold J.; Mattson, Mariena V.; Bowen, Wayne D.; Becketts, Karen; Xu, Heng; Rothman, Richard B.; Flippen-Anderson, Judith L.;

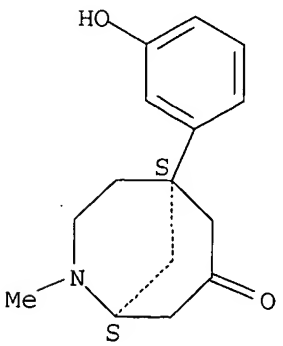
Rice, Kenner C.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(24), 4776-85
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

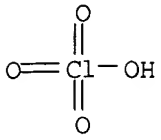
AB The determination of the structure and function of the σ receptor subtypes and their physiol. role(s) has been impeded by the unavailability of selective ligands. We have developed a new class of σ subtype selective receptor ligands that are (E)-8-benzylidene derivs. of the synthetic opioid (±)-, (+)-, and (-)-2-methyl-5-(3-hydroxyphenyl)morphans (1). The derivs. can be prepared by reaction of 1, (+)-1, and (-)-1 with the appropriate benzaldehyde under Claisen-Schmidt conditions. Incorporation of substituted (E)-8-benzylidene moieties onto the 7-keto precursor of (+)-2-methyl-5-(3-hydroxyphenyl)morphan, (+)-1, produces compds. which have between a 25- and 131-fold increase in affinity for the σ1 receptor subtype relative to the keto precursor (+)-1 (Ki = 762 nM, σ1). Substitution of an (E)-8-benzylidene moiety onto the 7-keto precursor of (-)-2-methyl-5-(3-hydroxyphenyl)morphan, (-)-1, produces compds. which have at least a 475-3906-fold increase in affinity for the σ2 receptor subtype relative to the keto precursor (-)-1 (Ki = 25 + 103 nM). This enhancement of σ2 receptor affinity is accompanied by substantial selectivity of all of these dextrorotatory products for the σ2 relative to the σ1 subtype (32-238-fold), and thus, they are among the most σ2 subtype selective compds. currently known. Furthermore, the σ1 subtype is highly enantioselective for the levorotatory isomers (41-1034-fold), whereas the σ2 subtype is only somewhat enantioselective for the dextrorotatory isomers (2.6-9.3-fold). All of these derivs. retain substantial affinity for the μ opioid receptor. Despite the high affinity of the dextrorotatory derivs. for the μ opioid receptor, the high affinity and selectivity for σ2 over σ1 sites will surely prove beneficial as tools for the delineation of the function and physiol. role of σ2 receptors.

IT **157752-16-4 157752-17-5 162060-90-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(preparation of (E)-8-benzylidene derivs. of 2-methyl-5-(3-hydroxyphenyl)morphans as selective ligands for σ2 receptor)

RN 157752-16-4 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



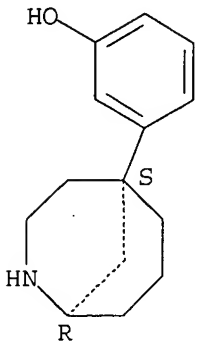


L6 ANSWER 28 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:792484 CAPLUS
DOCUMENT NUMBER: 123:218718
TITLE: Ligand selectivity of cloned human and rat opioid Mu receptors
AUTHOR(S): Brothman, Richard B.; Xu, Heng; Wang, Jia Bei; Partilla, John S.; Kayakiri, Hiroshi; Rice, Kenner C.; Uhl, George R.
CORPORATE SOURCE: Clinical Psychopharmacology Section, Laboratory of Medicinal Chemistry, Baltimore, MD, 21224, USA
SOURCE: Synapse (New York) (1995), 21(1), 60-4
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Opiate receptors play major roles in analgesic and euphoric effects of opiate drugs. Recent cloning of cDNAs encoding the rodent and human μ receptor revealed high homol. between the predicted receptors but also some sequence differences. To determine if these sequence differences produced significant changes in ligand-selectivity profiles, the authors assessed these profiles in expressing COS and CHO cell lines using the agonist ligand [125I]IOXY-AGO (5β-[125Iodo]-3,14-dihydroxy-17-methyl-4-5α-epoxymorphinan). This ligand's high specific activity (2200 Ci/mmol) and high affinity for μ opioid receptors generated high signal-to-noise ratio binding. The resulting ligand-selectivity profiles of the human and rat μ receptors reveal modest differences in affinities for morphine and naloxone in COS cells but not CHO cells. Ligand-selectivity profiles of the rat and human μ receptors were otherwise similar. Interesting differences between these data and data previously obtained with the peptide agonist [3H]DAMGO suggest that the peptide and alkaloid agonists may label different domains of the μ receptor.

IT **168135-17-9**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cloned human and rat opioid μ-receptor ligand selectivity)
RN 168135-17-9 CAPLUS
CN Phenol, 3-(1R,5S)-2-azabicyclo[3.3.1]non-5-yl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



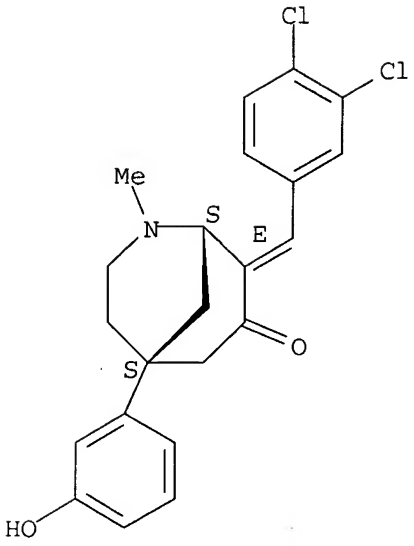

L6 ANSWER 29 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:596413 CAPLUS
DOCUMENT NUMBER: 123:75461
TITLE: CB-64D and CB-184: ligands with high σ2 receptor affinity and subtype selectivity
AUTHOR(S): Bowen, Wayne D.; Bertha, Craig M.; Vilner, Bertold J.; Rice, Kenner C.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: European Journal of Pharmacology (1995), 278(3), 257-60
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Four members of a novel class of sigma (σ) ligands were investigated for σ subtype selectivity. (-)-1S,5S- and (+)-1R,5R-(E)-8-Benzylidene-5-(3-hydroxyphenyl)-2-methylmorphan-7-one (CB-64L and CB-64D, resp.) exhibited σ1 Ki = 10.5 nM and 3063 nM; σ2 Ki = 154 nM and 16.5 nM, resp. The corresponding 3,4-dichloro derivs., (-)-1S,5S- and (+)-1R,5R-(E)-8-(3,4-dichlorobenzylidene)-5-(3-hydroxyphenyl)-2-Me morphan-7-one (CB-182 and CB-184, resp.) were also examined CB-182 ((-)-isomer) showed σ1 and σ2 Ki = 27.3 nM and 35.5 nM, resp., whereas CB-184 ((+)-isomer) exhibited σ1 and σ2 Ki = 7436 nM and 13.4 nM, resp. Thus, the two σ subtypes showed opposite enantioselectivity for these compds., with (-)>(+) at σ1 and (+)>(-) at σ2. Importantly, CB-64D and CB-184 showed high σ2 affinity and, resp., 185-fold and 554-fold selectivity for σ2 receptors over σ1. While high σ2 selectivity relative to σ1 was achieved with these compds., they both exhibited high affinity at mu (μ) opioid receptors (Ki = 37.6 nM and 4.5 nM, resp.). Despite this, CB-64D and CB-184 will be useful tools for further characterization of σ2 receptors.

IT **157752-18-6 157752-20-0 165307-46-0 165307-47-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CB-64D and CB-184: ligands with high σ2 receptor affinity and subtype selectivity)

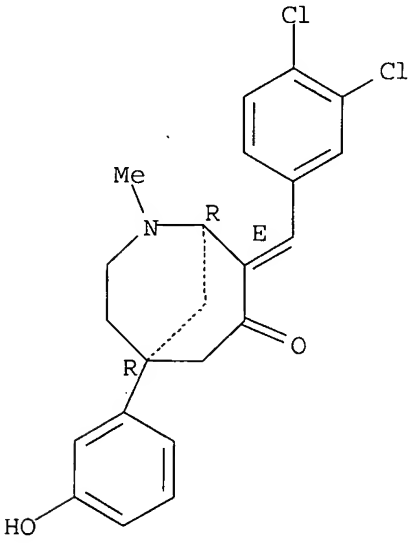
RN 157752-18-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (1S,5S,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



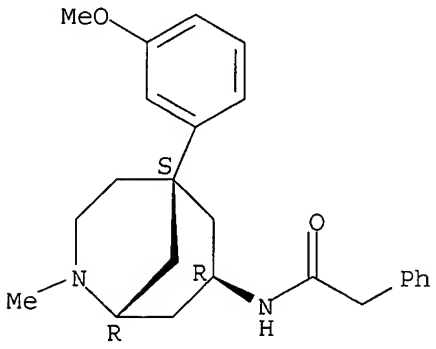

RN 165307-47-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 8-[(3,4-dichlorophenyl)methylene]-5-(3-hydroxyphenyl)-2-methyl-, (1R,5R,8E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.




L6 ANSWER 30 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:508230 CAPLUS
DOCUMENT NUMBER: 122:230141
TITLE: Probes for Narcotic Receptor-Mediated Phenomena. 20. Alteration of Opioid Receptor Subtype Selectivity of the 5-(3-Hydroxyphenyl)morphans by Application of the Message-Address Concept: Preparation of δ-Opioid Receptor Ligands
AUTHOR(S): Bertha, Craig M.; Flippen-Anderson, Judith L.; Rothman, Richard B.; Porreca, Frank; Davis, Peg; Xu, Heng; Becketts, Karen; Cha, Xian-Yuan; Rice, Kenner C.

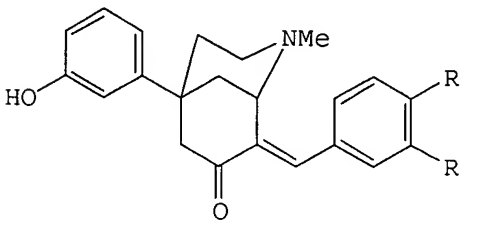
Relative stereochemistry.



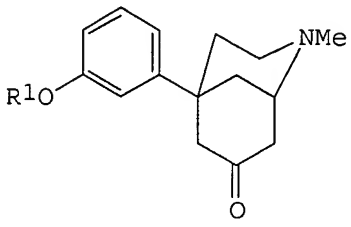

● HBr

L6 ANSWER 31 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1994:605756 CAPLUS
DOCUMENT NUMBER: 121:205756
TITLE: A Marked Change of Receptor Affinity of the 2-Methyl-5-(3-hydroxyphenyl)morphans upon Attachment of an (E)-8-Benzylidene Moiety: Synthesis and Evaluation of a New Class of σ Receptor Ligands
AUTHOR(S): Bertha, Craig M.; Mattson, Mariena V.; Flippen-Anderson, Judith L.; Rothman, Richard B.; Xu, Heng; Cha, Xian-Yuan; Becketts, Karen; Rice, Kenner C.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 20892, USA
SOURCE: Journal of Medicinal Chemistry (1994), 37(19), 3163-70
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



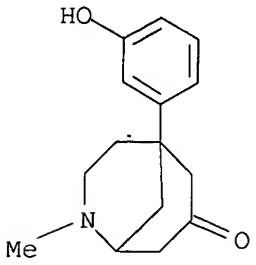

I




II

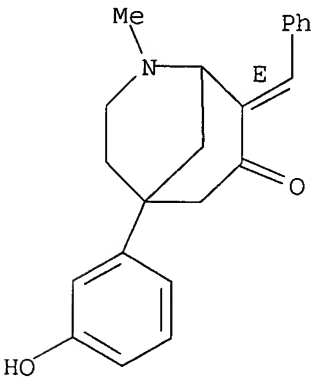
AB The (E)-8-benzylidene and (E)-8-(3,4-dichlorobenzylidene), 7-ketone derivs., I (R = H, Cl), of the synthetic opiate 2-methyl-5-(3-hydroxyphenyl)morphan [5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane], were synthesized from II (R1 = H, Me) via the Claisen-Schmidt reaction. The corresponding enantiomers of I were obtained in >99% optical purity from the optical isomers of II (R1 = H), resolved with the O,O'-dibenzoyltartaric acids. The absolute configurations of the enantiomers of II (R1 = H) were determined The determination of the regioisomer

INDEX NAME)

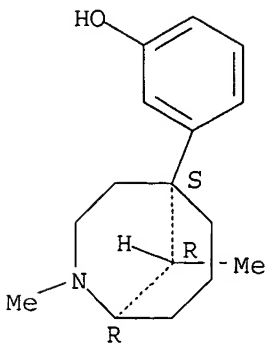



IT **157668-79-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, crystal structure, and opioid binding activity of)
RN 157668-79-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-hydroxyphenyl)-2-methyl-8-(phenylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.




L6 ANSWER 32 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:125 CAPLUS
DOCUMENT NUMBER: 120:125
TITLE: Conformational analysis of the opioid phenylmorphan and its 9α-methyl analog in solution using high-resolution nuclear magnetic resonance spectroscopy
AUTHOR(S): DiMeglio, Christine M.; Froimowitz, Mark; Makriyannis, Alexandros
CORPORATE SOURCE: Sch. Pharm., Univ. Connecticut, Storrs, CT, 06269, USA
SOURCE: Pharmaceutical Research (1993), 10(8), 1200-5
CODEN: PHREEB; ISSN: 0724-8741
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

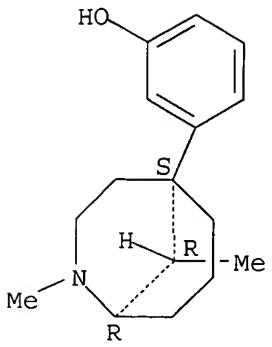



L6 ANSWER 33 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:256 CAPLUS
DOCUMENT NUMBER: 118:256
TITLE: Absolute configuration and conformation of the pure opioid antagonist (+)-2,9α-dimethyl-5-(m-hydroxyphenyl)morphan
AUTHOR(S): Froimowitz, Mark; Pangborn, Walter; Cody, Vivian
CORPORATE SOURCE: Alcohol Drug Res. Cent., McLean Hosp., Belmont, MA, 02178-9106, USA
SOURCE: Chirality (1992), 4(6), 377-83
CODEN: CHRLEP; ISSN: 0899-0042
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (+)-2,9α-Dimethyl-5-(m-hydroxyphenyl)morphan is the only phenylmorphan analog whose affinity for opioid κ-receptors is greater than its affinity for opioid μ-receptors. Pharmacol., the compound is a pure opioid antagonist devoid of agonist activity in in vivo assays of antinociception. The absolute configuration of the compound has been determined to be (1R,5S,9R) from an X-ray crystallog. study of the chloride salt. Thus, the absolute configuration corresponds to that of the atypical opioid agonist (-)-phenylmorphan while the weak atypical agonist (-)-2,9α-dimethyl-5-(m-hydroxyphenyl)morphan corresponds to the potent morphine-like (+)-phenylmorphan. The preferred orientations of the Ph ring for the two stereoisomers were determined using the mol. mechanics program MM2-87 and found to vary from that of the two parent compds. The atypical properties of the two 9α-Me analogs is consistent with an opioid ligand model which proposes that morphine-like properties require a particular range of Ph orientations. There was good agreement between the structure obtained from X-ray crystallog. and computed with the MM2-87 program.

IT **88550-31-6**
RL: PRP (Properties)
(configuration and conformation of, crystal structure in relation to)
RN 88550-31-6 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, anti-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown.



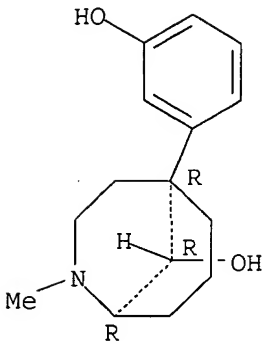
● HCl

L6 ANSWER 34 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:227659 CAPLUS
DOCUMENT NUMBER: 116:227659
TITLE: Phenylmorphans and analogs: opioid receptor subtype selectivity and effect of conformation on activity
AUTHOR(S): Froimowitz, Mark; Pick, Chaim G.; Pasternak, Gavril W.
CORPORATE SOURCE: Alcohol Drug Abuse Res. Cent., McLean Hosp., Belmont, MA, 02178, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(9), 1521-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The morphine-like (+)-phenylmorphan, the atypical (-)-enantiomer, and some analogs were tested in receptor binding assays selective for opioid μ1, μ2, δ, κ1, and κ3 receptors. The affinities of all of the compds. except one, including the atypical (-)-phenylmorphan, were greatest for μ1 and μ2 receptors. The only exception was the (+)-9α-Me analog which had slightly greater affinity for the κ1 receptor. The selective receptor binding assays provide evidence that opioids in which the Ph ring is constrained to be equatorial on the piperidine ring can have considerable affinity for μ receptors. In addition, the analgesic dose-response curves were determined for (+)- and (-)-phenylmorphan using the mouse tail-flick assay with the (+)-enantiomer being 7-fold more potent. Pretreatment with the selective opioid antagonists β-FNA (μ1 and μ2), naloxonazine (μ1), nor-BNI (κ1), and naltrindole (δ) suggests that the antinociceptive activity of both enantiomers is mediated through μ receptors. The pretreatment with naloxonazine, which attenuated the antinociceptive effect, shows that both (+)- and (-)-phenylmorphans are μ1 agonists, while intrathecal administration shows that both are μ2 agonists. Conformational energy calcns. on the compds. were also performed using the MM2-87 program. Consistent with previous conformational results for the phenylmorphans, the most potent antinociceptive compds. preferred a particular orientation of the Ph ring.

IT **28623-81-6 28623-84-9 88550-29-2 88550-30-5 88550-32-7 95689-22-8 95689-26-2**
RL: BIOL (Biological study)
(analgesic activity and opioid receptor subtype selectivity of)

RN 28623-81-6 CAPLUS
CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

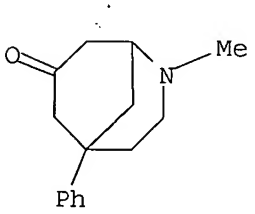



L6 ANSWER 35 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:174489 CAPLUS
DOCUMENT NUMBER: 116:174489
TITLE: Carbon-13 NMR chemical shift assignments for substituted 2-azabicyclo[3.3.1]nonan-7-ones
AUTHOR(S): Casamitjana, Nuria; Bonjoch, Josep; Gracia, Jordi; Bosch, Joan
CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, 08028, Spain
SOURCE: Magnetic Resonance in Chemistry (1992), 30(2), 183-5
CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE: Journal
LANGUAGE: English

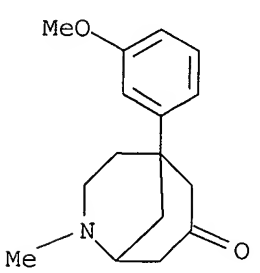
AB The 13C NMR spectra of 26 substituted 2-azabicyclo[3.3.1]nonan-7-ones are reported, providing a diagnostic method for the stereochem. elucidation of the relative configuration of these products.

IT **140165-64-6 140165-65-7**
RL: PRP (Properties)
(carbon-13 NMR of)

RN 140165-64-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)

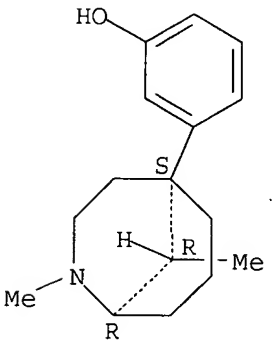



RN 140165-65-7 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)



L6 ANSWER 36 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:135894 CAPLUS
DOCUMENT NUMBER: 114:135894
TITLE: Evaluation of new compounds for opioid activity
AUTHOR(S): Woods, J.; Medzihradsky, F.; Smith, C.; Winger, G.; France, C.
CORPORATE SOURCE: USA
SOURCE: NIDA Research Monograph (1988), 90(Probl. Drug Depend., 1988), 421-67
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The opioid activity of different compds. tested in different exptl. systems are described.
IT **88550-32-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opioid activity of, evaluation of)
RN 88550-32-7 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti-(-)- (9CI) (CA INDEX NAME)

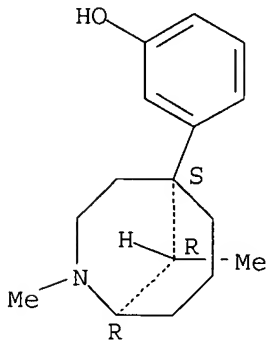
Rotation (-). Absolute stereochemistry unknown.



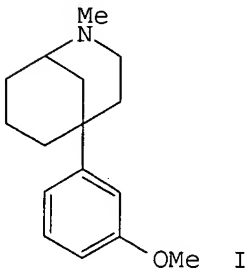

L6 ANSWER 37 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:111859 CAPLUS
Correction of: 1988:486100
DOCUMENT NUMBER: 112:111859
Correction of: 109:86100
TITLE: Biological evaluation of compounds for their physical dependence potential and abuse liability. X. Drug testing programs of the Committee on Problems of Drug Dependence, Inc. (1986)
AUTHOR(S): Jacobson, Arthur E.
CORPORATE SOURCE: Lab. Chem., Natl. Inst. Diabetes Dig. Kidney Dis., Bethesda, MD, 20892, USA
SOURCE: NIDA Research Monograph (1987), 76(Probl. Drug Depend., 1986), 370-91
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A report is given on the drug-testing programs of the Committee on Problems of Drug Dependence, and new and lit. data are presented from studies of the dpendency potential of a large number of drugs, including epoxymorphinans, phenylmorphans, benzomorphans, methadone-like compds., pethidines, fentanyls, etc.

IT **88550-29-2**
RL: PRP (Properties)
(abuse and dependence potential of)
RN 88550-29-2 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.




L6 ANSWER 38 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:8444 CAPLUS
DOCUMENT NUMBER: 110:8444
TITLE: Functionalized 2-azabicyclo[3.3.1]nonanes. VIII. New synthesis of 5-phenylmorphans
AUTHOR(S): Bonjoch, Josep; Casamitjana, Nuria; Bosch, Joan
CORPORATE SOURCE: Fac. Pharm., Univ. Barcelona, Barcelona, 08028, Spain
SOURCE: Tetrahedron (1988), 44(6), 1735-41
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:8444
GI

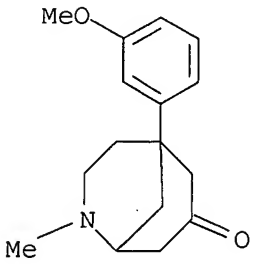


I

AB A new procedure for the synthesis of 2-azabicyclo[3.3.1]nonanes, e.g. I, by intramol. cyclization of 4-acetonyl-2-piperidinecarbonitriles under acidic conditions is described. The procedure allows the preparation of the pharmacol. interesting 5-phenylmorphans and involves the initial formation of 1-methyl-4-acetonylidenepiperidine, conjugate addition of a diaryl-cuprate, and cyclization of the resulting 4-acetonylpiperidine by way of the corresponding 2-cyano derivative

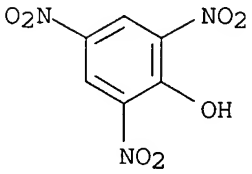
IT **140165-65-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)

CRN 140165-65-7
CMF C16 H21 N O2

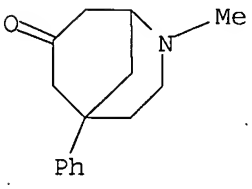



CM 2

CRN 88-89-1
CMF C6 H3 N3 O7




RN 140165-64-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-7-one, 2-methyl-5-phenyl- (9CI) (CA INDEX NAME)




L6 ANSWER 39 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:583743 CAPLUS
DOCUMENT NUMBER: 105:183743
TITLE: Evaluation of new compounds for opioid activity (1985)
AUTHOR(S): Woods, James H.; Medzihradsky, Fedor; Smith, Charles B.; Winger, Gail D.; Gmerek, Debra E.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Michigan, Ann Arbor, MI, 48109-0010, USA
SOURCE: NIDA Research Monograph (1986), 67(Probl. Drug Depend.), 453-89
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The opioid-like activity of 36 compds. (benzomorphans, xylidines, morphinans, peptides, phenylpiperazines, etc.) was evaluated and the data were summarized in this report. The test procedures included drug discrimination, dependence liability, and i.v. self-administration in monkeys, displacement of [3H]etorphine from rat cerebral membranes, and inhibition of twitch in elec. driven guinea pig ileum and mouse vas

deferens.

IT **95689-23-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opioid activity of)

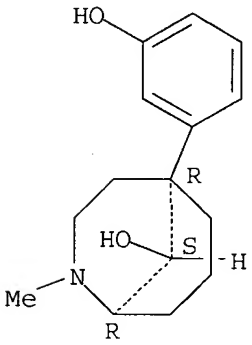
RN 95689-23-9 CAPLUS

CN Benzeneacetic acid, α-hydroxy-, compd. with syn-5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonan-9-ol (1:1) (9CI) (CA INDEX NAME)

CM 1

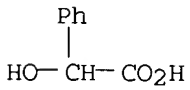
CRN 95689-22-8
CMF C15 H21 N O2

Relative stereochemistry.



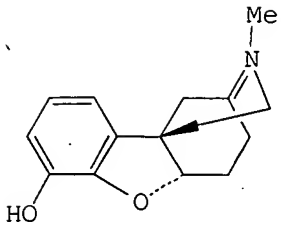

CM 2

CRN 90-64-2
CMF C8 H8 O3

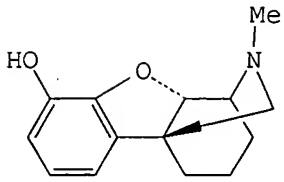



L6 ANSWER 40 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1985:160031 CAPLUS
DOCUMENT NUMBER: 102:160031
TITLE: Probes for narcotic receptor mediated phenomena 3. Oxide bridged 5-phenylmorphans
AUTHOR(S): Burke, Terrence R., Jr.; Jacobson, Arthur E.; Rice, Kenner C.; Weissman, Ben Avi; Silverton, James V.
CORPORATE SOURCE: Lab. Chem., NIH, MD, USA
SOURCE: NIDA Research Monograph (1984), 49, 109-13
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
GI




I




II

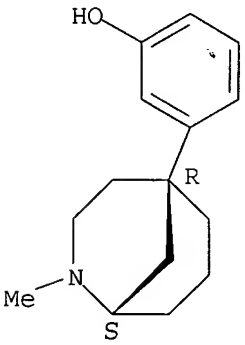
AB Oxide bridged 5-phenylmorphans (I and II) were prepared and tested for analgesic activity as well as opiate receptor binding properties. The phenylmorphans had no analgesic activity. II exhibited appreciable binding to rat brain homogenate. Structural requirement of the drugs binding to opiate receptors is discussed.

IT **28623-81-6 28623-84-9**
RL: PROC (Process)
(analgesic activity and opiate receptor binding of)

RN 28623-81-6 CAPLUS

CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

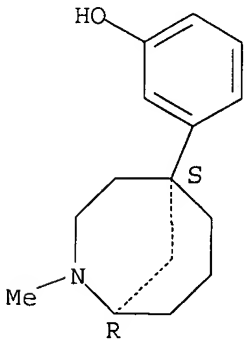
Absolute stereochemistry. Rotation (+).



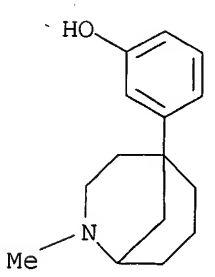

RN 28623-84-9 CAPLUS

CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

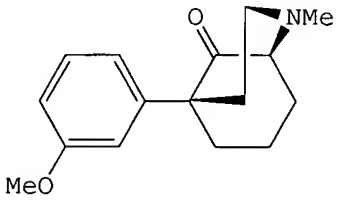
Absolute stereochemistry. Rotation (-).



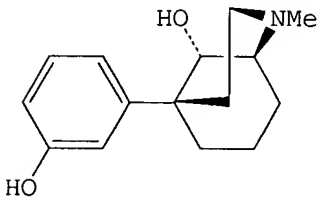
ACCESSION NUMBER: 1985:159988 CAPLUS
DOCUMENT NUMBER: 102:159988
TITLE: Demonstration and affinity labeling of a stereoselective binding site for a benzomorphan opiate on acetylcholine receptor-rich membranes from Torpedo electroplaque
AUTHOR(S): Oswald, Robert E.; Pennow, Nancy N.; McLaughlin, James T.
CORPORATE SOURCE: New York State Coll. Vet. Med., Cornell Univ., Ithaca, NY, 14853, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(3), 940-4
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction of an optically pure benzomorphan opiate, (-)-N-allyl-N-normetazocine [(-)-ANMC] [14198-28-8], with the nicotinic acetylcholine receptor from Torpedo electroplaque was studied by using radioligand binding and affinity labeling. The binding was complex with at least 2 specific components having equilibrium dissociation consts. of 0.3 μM and 2 μM. The affinity of the higher affinity component was decreased by carbamoylcholine [462-58-8] but not by α-bungarotoxin [11032-79-4]. The effect of carbamoylcholine was not blocked by α-bungarotoxin. In comparison, the affinity of [3H]phencyclidine [77-10-1], a well-characterized ligand for a high-affinity site for noncompetitive blockers on the acetylcholine receptor, is increased by carbamoylcholine and the increase is blocked by α-bungarotoxin. The binding of (-)-[3H]ANMC was inhibited by a number of other benzomorphans, with (-)-isomers being 4- to 5-fold more potent than (+)-isomers. Phencyclidine inhibits the binding of (-)-[3H]ANMC to its high-affinity site by a mechanism that is not competitive. UV-catalyzed affinity labeling indicated that the high-affinity-binding site for (-)-[3H]ANMC is at least partially associated with the δ subunit. Tryptic degradation of the Torpedo marmorata δ chain suggested that (-)-ANMC labeled a 16,000-dalton COOH-terminal portion of the subunit. In contrast, 5-azidotrimethisoquin [75041-53-1], a photoaffinity label of the high-affinity site for noncompetitive blockers, labels a 47,000-dalton NH2-terminal fragment of the δ subunit. Thus, (-)-[3H]ANMC binds to sites completely distinct from the binding sites for acetylcholine. The high-affinity-binding site for (-)-ANMC and that for phencyclidine and 5-azidotrimethisoquin are allosterically coupled but are regulated differently and are probably phys. distinct.
IT **27107-68-2**
RL: BIOL (Biological study)
(normetazocine binding to acetylcholine receptor rich membrane response to, in Torpedo electroplaque)
RN 27107-68-2 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



L6 ANSWER 42 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:149088 CAPLUS
DOCUMENT NUMBER: 102:149088
TITLE: 9α- and 9β-hydroxyphenylmorphans
AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Jacobson, Arthur E.; Aceto, Mario D.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
SOURCE: Journal of Pharmaceutical Sciences (1984), 73(12), 1867-8
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI




I



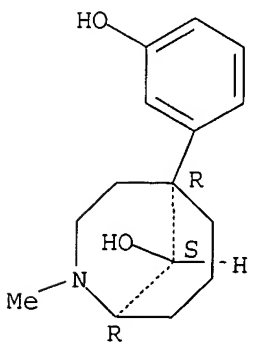

III

AB Platinum oxide hydrogenation of 5-m-methoxyphenyl-2-methyl-9-oxomorphan (I) gave the 9α-hydroxy racemate whose phenolic analog (II) is a strong antinociceptive agent, fully supportive of morphine dependence in rhesus monkeys. The di-O-acetyl derivative of II was similar to II in its profile of activity. The diastereoisomer of II, obtained by hydrogenation of the methobromide of I, extrusion of Me bromide, and O-demethylation of the resultant free base, was almost inactive antinociceptively and did not suppress withdrawal symptoms in morphine-dependent monkeys. The orientation of the C-9 hydroxyl groups was deduced from spectral data and by analogy.

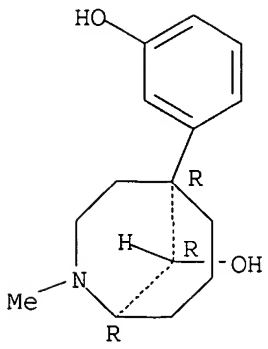
IT **95689-22-8P 95689-23-9P 95689-24-0P**
**95689-25-1P 95689-26-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antinociceptive activity of)

RN 95689-22-8 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-9-ol, 5-(3-hydroxyphenyl)-2-methyl-, syn- (9CI) (CA INDEX NAME)

Relative stereochemistry.



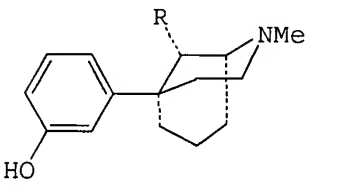

RN 95689-23-9 CAPLUS



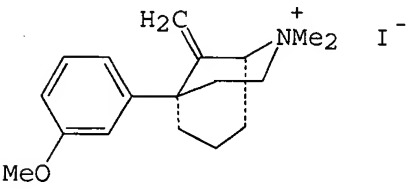
● HCl

L6 ANSWER 43 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

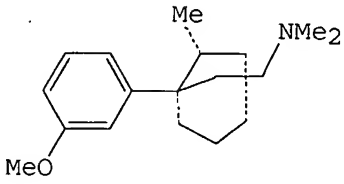
ACCESSION NUMBER: 1984:121413 CAPLUS
DOCUMENT NUMBER: 100:121413
TITLE: Racemic and optically active 2,9-dimethyl-5-(m-hydroxyphenyl)morphans and pharmacological comparison with the 9-demethyl homologs
AUTHOR(S): Awaya, Hiroyoshi; May, Everette L.; Aceto, Mario D.; Merz, Herbert; Rogers, Michael E.; Harris, Louis S.
CORPORATE SOURCE: Dep. Pharmacol., Med. Coll. Virginia, Richmond, VA, 23298, USA
SOURCE: Journal of Medicinal Chemistry (1984), 27(4), 536-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



IV

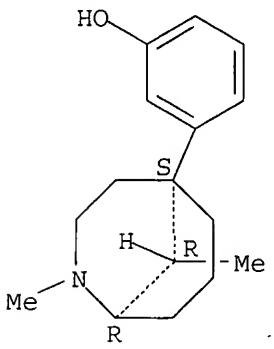


V

AB Dimethyl(hydroxyphenyl)morphan I (R = Me)(II) was prepared from 5-(m-methoxyphenyl)-2-methyl-9-oxomorphan and resolved into its enantiomers. The α-orientation of the C-9 Me group was derived from studies of induced NMR shifts. (+)-II has inappreciable agonist (antinociceptive) activity in mice, and (-)-II shows codeine-like potency in the hot-plate and writhing tests only. The 9-demethyl homologs I (R = H)(III) are strong agonists, about as potent as morphine in these tests as well as in the tail-flick assay. (±)-II and (+)-II, but not (-)-I,

IT **88550-33-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 88550-33-8 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, anti-(-)- (9CI) (CA INDEX NAME)

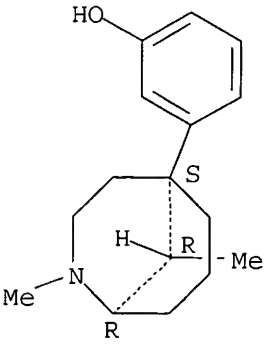
Rotation (-). Absolute stereochemistry unknown.



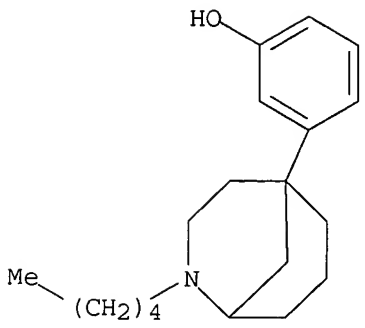

● HCl

IT **88550-29-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, resolution, and narcotic antagonist and agonist activities of)
RN 88550-29-2 CAPLUS
CN Phenol, 3-(2,9-dimethyl-2-azabicyclo[3.3.1]non-5-yl)-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.



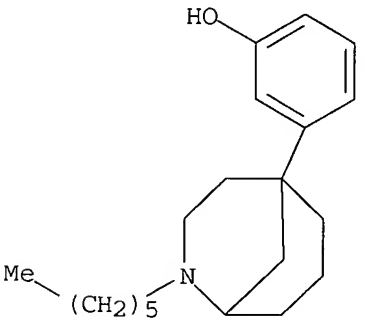

L6 ANSWER 44 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:27684 CAPLUS
DOCUMENT NUMBER: 98:27684
TITLE: Biological evaluation of compounds for their dependence liability. V. Drug testing program of the Committee on Problems of Drug Dependence, Inc. (1981)
AUTHOR(S): Jacobson, A. E.
CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Diabetes Dig. Kidney Dis., Bethesda, MD, 20205, USA
SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 331-7




● HCl

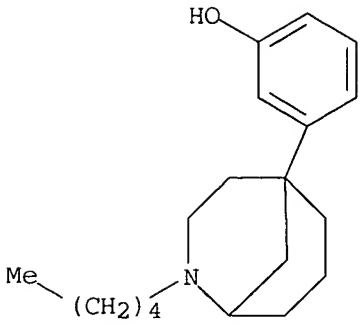
RN 83502-18-5 CAPLUS
CN Phenol, 3-(2-hexyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).




● HCl

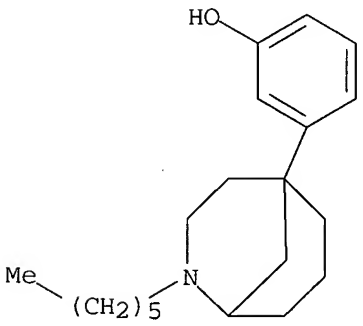
L6 ANSWER 45 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:592941 CAPLUS
DOCUMENT NUMBER: 97:192941
TITLE: Dependence studies of new compounds in the rhesus monkey, rat, and mouse (1981)
AUTHOR(S): Aceto, M. D.; Harris, L. S.; May, E. L.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, 23298, USA
SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 338-80
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sixty-six compds. were tested for dependence in the rhesus monkey, rat, and mouse by various methods.
IT **27107-49-9 27107-50-2 83502-15-2 83502-16-3 83502-17-4 83502-18-5**
RL: BIOL (Biological study)




● HCl

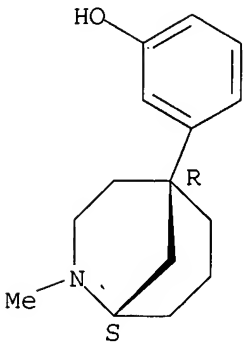
RN 83502-18-5 CAPLUS
CN Phenol, 3-(2-hexyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



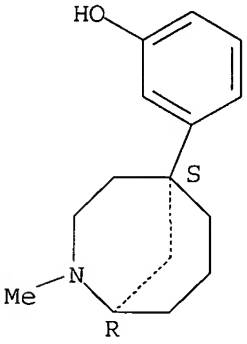

● HCl

L6 ANSWER 46 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:555939 CAPLUS
DOCUMENT NUMBER: 97:155939
TITLE: Structural requirements for affinity and intrinsic activity at the opiate receptor defined in 4-phenylpiperidine and related series
AUTHOR(S): Zimmerman, D. M.; Smits, S. E.; Hynes, M. D.; Cantrell, B. E.; Reamer, M.; Nickander, R.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: NIDA Research Monograph (1982), Volume Date 1981, 41, 112-18
CODEN: MIDAD4; ISSN: 0361-8595
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

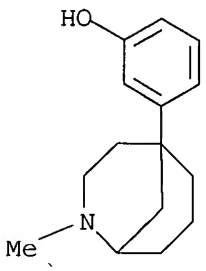



RN 28623-84-9 CAPLUS
CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L6 ANSWER 47 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:604248 CAPLUS
DOCUMENT NUMBER: 95:204248
TITLE: Phenylpropylamino groups of morphine analgesics plotted with a computer
AUTHOR(S): Brouant, P.; Soyfer, J. C.
CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, F 13385/5, Fr.
SOURCE: Annales Pharmaceutiques Francaises (1981), 39(2), 125-31
CODEN: APFRAD; ISSN: 0003-4509
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The conformational variations of the phenylpropylamino group of morphine and related analgesics were plotted with a computer on the basis of crystallog. data. The analgesic activity was related to the conformational variations.
IT **76580-81-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation of phenylpropylamino group in, computer-plotted, analgesic activity in relation to)
RN 76580-81-9 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide (9CI) (CA INDEX NAME)



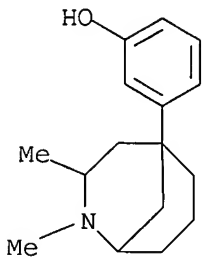

● HBr

L6 ANSWER 48 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:83962 CAPLUS
DOCUMENT NUMBER: 94:83962
TITLE: Phenylmorphan derivatives
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 55124768 | A2 | 19800926 | JP 1980-32566 | 19800311 |
| FR 2451368 | A1 | 19801010 | FR 1980-5179 | 19800307 |
| FR 2451368 | B1 | 19830318 | | |
| BE 882152 | A1 | 19800910 | BE 1980-9743 | 19800310 |
| HU 22162 | O | 19820428 | HU 1980-561 | 19800310 |
| HU 179836 | B | 19821228 | | |
| CA 1148150 | A1 | 19830614 | CA 1980-347364 | 19800310 |
| EP 18077 | A2 | 19801029 | EP 1980-300746 | 19800311 |
| EP 18077 | A3 | 19801126 | | |
| R: DE, GB, NL, SE | | | | |
| GB 2045248 | A | 19801029 | GB 1980-8172 | 19800311 |
| GB 2045248 | B2 | 19830505 | | |
| EP 59989 | A1 | 19820915 | EP 1982-102714 | 19800311 |
| R: DE, GB, NL, SE | | | | |
| US 4278797 | A | 19810714 | US 1980-150763 | 19800519 |
| GB 2111976 | A1 | 19830713 | GB 1982-27192 | 19820923 |

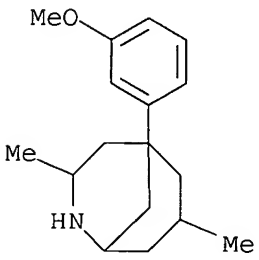
PRIORITY APPLN. INFO.:
US 1979-19527 A 19790312
EP 1980-300746 A 19800311
GB 1980-8172 A3 19800311

OTHER SOURCE(S): CASREACT 94:83962
GI

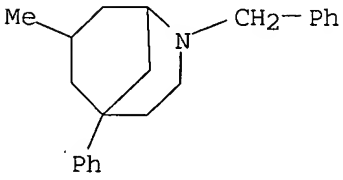


● HBr

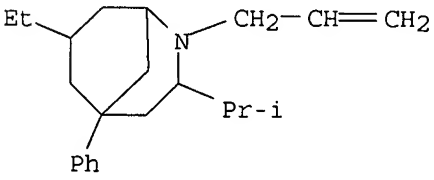
RN 76580-91-1 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-3,7-dimethyl- (9CI) (CA INDEX NAME)



RN 76580-92-2 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 7-methyl-5-phenyl-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

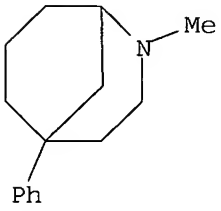


RN 76580-93-3 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 7-ethyl-3-(1-methylethyl)-5-phenyl-2-(2-propenyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 49 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:639720 CAPLUS
DOCUMENT NUMBER: 93:239720

TITLE: Application of metalated enamines to alkaloid synthesis. An expedient approach to the synthesis of morphine-based analgesics
AUTHOR(S): Evans, D. A.; Mitch, C. H.; Thomas, R. C.; Zimmerman, D. M.; Robey, R. L.
CORPORATE SOURCE: Dep. Chem., California Inst. Technol., Pasadena, CA, 91125, USA
SOURCE: Journal of the American Chemical Society (1980), 102(18), 5955-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Catalytic hydrogenation of the phenylpiperidine I (R = CH2CH:CH2), obtained by treatment of 1-methyl-4-phenyl-1,2,4,5-tetrahydropyridine with BuLi followed by H2C:CHCH2Br, gave the piperidine II. I (R = CH2CH:CH2) was treated with H3PO4-HCO2H to give the cyclic enamine, which was hydrogenated to give the phenylmorphan III. I [R = (CH2)4Cl] was cyclized with Na I to give the octahydroisoquinoline IV, which hydrogenated to give the corresponding cis- or trans-decahydroisoquinoline depending on hydrogenation conditions. IV was treated with etheral perchloric acid to give the trans fused immonium perchlorate which was converted to the morphinan V.
IT **74904-15-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 74904-15-7 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride (9CI) (CA INDEX NAME)




● HCl

L6 ANSWER 50 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:532662 CAPLUS
DOCUMENT NUMBER: 93:132662
TITLE: Radiocrystallographic study of variations in skeletal conformation in morphine analgesics
AUTHOR(S): Brouant, P.; Soyfer, J. C.
CORPORATE SOURCE: Lab. Pharm. Chim., Fac. Pharm., Marseille, 13385/4, Fr.
SOURCE: Annales Pharmaceutiques Francaises (1979), 37(9-10), 461-8
CODEN: APFRAD; ISSN: 0003-4509
DOCUMENT TYPE: Journal
LANGUAGE: French
AB Eight parameters, defined from the crystallog. coordinates, for 21 analgesics containing the phenylpropylamine group, were based on the distance between the N atom and a quaternary C atom center, various planes or centers in aromatic rings. The distances formed 4 distinct sets which were

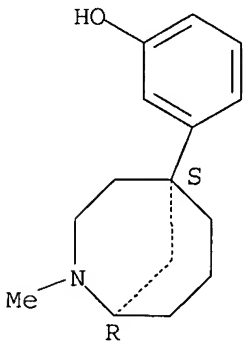
related to their physiol. activity. The conformations of the morphine-like analgesics was discussed.

IT **53467-24-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(conformation and crystal and mol. structure of, analgesic activity in)

RN 53467-24-6 CAPLUS

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-(9CI) (CA INDEX NAME)

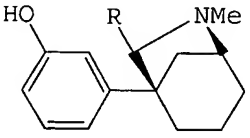
Absolute stereochemistry. Rotation (-).




● HBr

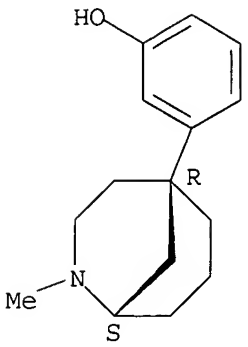
L6 ANSWER 51 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:50482 CAPLUS
DOCUMENT NUMBER: 86:50482
TITLE: Azabicycloalkanes as analgetics. 3. Structure-activity relations of 1-phenyl-6-azabicyclo[3.2.1]octanes and absolute stereochemistry of (+)-1-(3-hydroxyphenyl)-6-methyl-6-azabicyclo[3.2.1]octane and its 7-endo-methyl derivative
AUTHOR(S): Takeda, Mikio; Inoue, Hirozumi; Noguchi, Katsuyuki; Honma, Yasushi; Kawamori, Masatoshi; Tsukamoto, Goro; Yamawaki, Yasuhiko; Saito, Seiichi; Aoe, Keiichi; et al.
CORPORATE SOURCE: Res. Lab., Tanabe Seiyaku Co. Ltd., Japan
SOURCE: Journal of Medicinal Chemistry (1977), 20(2), 221-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 86:50482
GI




I, R=Me
II, R=H

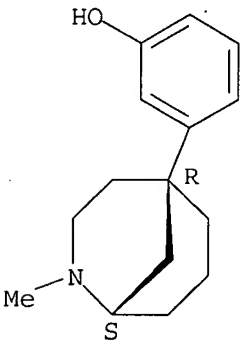
AB A series of 53 1-phenyl-6-azabicyclo[3.2.1]octanes was tested for analgesic and narcotic antagonist activities and structure-activity




● HCl

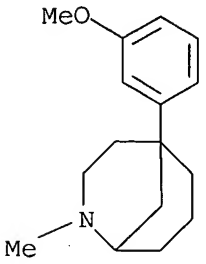
RN 28623-81-6 CAPLUS
CN Phenol, 3-[(1S,5R)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



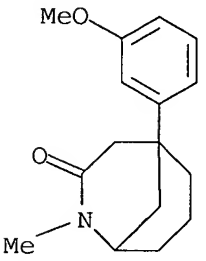

L6 ANSWER 52 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:51660 CAPLUS
DOCUMENT NUMBER: 82:51660
TITLE: Improved synthesis and additional pharmacology of the potent analgetic (-)-5-m-hydroxyphenyl-2-methylmorphan
AUTHOR(S): Rogers, Michael E.; May, Everette L.
CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Medicinal Chemistry (1974), 17(12), 1328-30
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The title compound (I) [**27107-68-2**] (16 mg/kg/day s.c.) produced very slight phys. dependence in Rhesus monkeys. Nalorphine and naloxone did not precipitate withdrawal symptoms in monkeys receiving I. At 32 mg/kg, I produced convulsions in monkeys. The 24-hr LD50 of I in mice was 137 mg/kg s.c. The yield of I in the previously reported synthesis (E. L. May and J. G. Murphy, 1955) was improved by changing the conditions for dimethylaminoethylation of 2-m-methoxyphenylcyclohexanone (II) [15547-89-4] and improving the resolution procedure. An alternative synthesis of I was described in which II was alkylated with Et

(9CI) (CA INDEX NAME)




● HBr

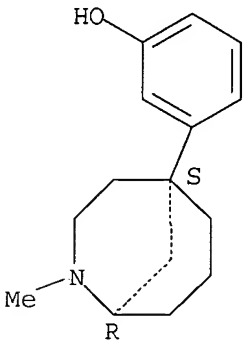
IT **53661-48-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reduction of)
RN 53661-48-6 CAPLUS
CN 2-Azabicyclo[3.3.1]nonan-3-one, 5-(3-methoxyphenyl)-2-methyl- (9CI) (CA INDEX NAME)




L6 ANSWER 53 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:25673 CAPLUS
DOCUMENT NUMBER: 82:25673
TITLE: Stereochemistry and absolute configuration of the analgesic agonist-antagonist (-)-5-m-hydroxyphenyl-2-methylmorphan
AUTHOR(S): Cochran, Todd G.
CORPORATE SOURCE: Sch. Pharm., Duquesne Univ., Pittsburgh, PA, USA
SOURCE: Journal of Medicinal Chemistry (1974), 17(9), 987-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Addnl. data considered in abstracting and indexing are available from a source cited in the original document. The absolute configuration of (-)-5-m-hydroxyphenyl-2-methylmorphan-HBr (I-HBr) [**53467-24-6**] was established as 1R, 5S by single-crystal x-ray anal. Both rings of the azabicyclononane system exist in chair conformations with the Ph and Me substituents equatorial. The distance between the cationic N and the aromatic ring is 5.66 Å. The relation between conformation and activity and receptor interaction was discussed.
IT **53467-24-6**
RL: PRP (Properties)
(absolute configuration of)

RN 53467-24-6 CAPLUS
CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, hydrobromide, (1R)-(9CI) (CA INDEX NAME)

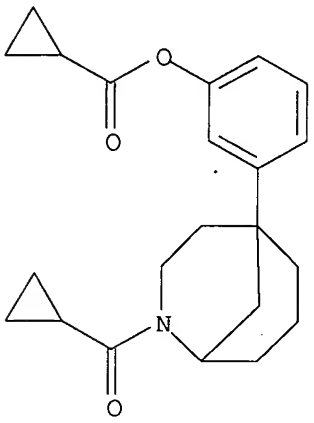
Absolute stereochemistry. Rotation (-).



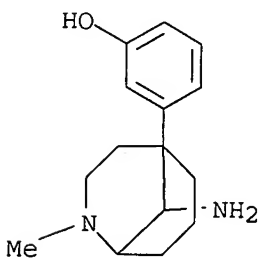

● HBr

L6 ANSWER 54 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1974:91126 CAPLUS
DOCUMENT NUMBER: 80:91126
TITLE: Phenylmorphan agonists-antagonists
AUTHOR(S): Ong, Helen H.; Ohishi, Tokuro; May, Everette L.
CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Medicinal Chemistry (1974), 17(1), 133-4
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (+)-5-(M-hydroxyphenyl)-2-propylmorphan-HBr (I) [**51264-07-4**], (+)-2-allyl-5-(m-hydroxyphenyl)morphan-HBr (II) [**51264-08-5**], and (+)-2-(cyclopropylmethyl)-5-(m-hydroxyphenyl)morphan-HBr (III) [**51264-09-6**] and the corresponding racemates were prepared and tested as analgesics. I and II were prepared by alkylation of (+)-5-(m-hydroxyphenyl)morphan (IV) [**51264-10-9**], while III was prepared by acylation of IV, followed by LiAlH4 reduction The analgesic activities of I, II, and III were 2-3 times higher than the corresponding racemates in the Nilsen test. With the hot plate test, I was 3 times more potent than its racemate. Analgesic and antagonist activities of the phenylmorphan derivative isomers were related to nalorphine-HCl [57-29-4], pentazocine-HCl [2276-52-0], and morphine sulfate [64-31-3].
IT **51596-46-4 51596-47-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(demethylation of)
RN 51596-46-4 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-, hydrobromide (9CI) (CA INDEX NAME)

RN 51596-51-1 CAPLUS
CN Cyclopropanecarboxylic acid, 3-[2-(cyclopropylcarbonyl)-2-azabicyclo[3.3.1]non-5-yl]phenyl ester (9CI) (CA INDEX NAME)

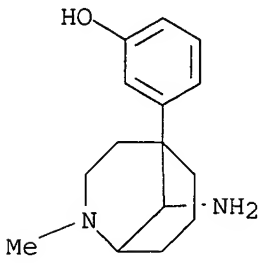


L6 ANSWER 55 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:140587 CAPLUS
DOCUMENT NUMBER: 76:140587
TITLE: Photocyclizations. II. Synthesis of iminoethanophenanthridine (seven-membered ring) homologs
AUTHOR(S): Ong, Helen H.; May, Everette L.
CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Organic Chemistry (1972), 37(5), 712-16
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Photolysis of 9-cis-chloroacetamino-5-(m-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane gave both ortho and para ring closure to propanopyridobenzazepinones (I and II) whose structures were deduced from mass and NMR spectral data and by chemical evidence.
IT **32969-96-3P 32969-97-4P 32969-98-5P 33068-03-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 32969-96-3 CAPLUS
CN Phenol, 3-(9-amino-2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)



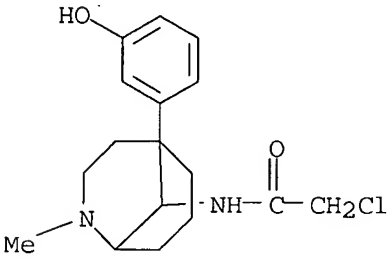
RN 32969-97-4 CAPLUS

CN Phenol, 3-(9-amino-2-methyl-2-azabicyclo[3.3.1]non-5-yl)-, dihydrobromide (9CI) (CA INDEX NAME)

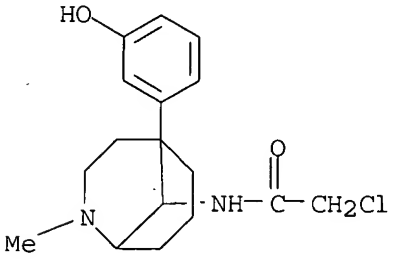


●2 HBr

RN 32969-98-5 CAPLUS
CN Acetamide, 2-chloro-N-[5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]- (9CI) (CA INDEX NAME)



RN 33068-03-0 CAPLUS
CN Acetamide, 2-chloro-N-[5-(3-hydroxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

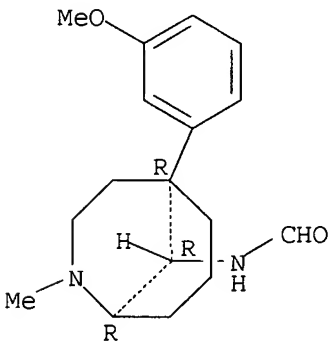


● HCl

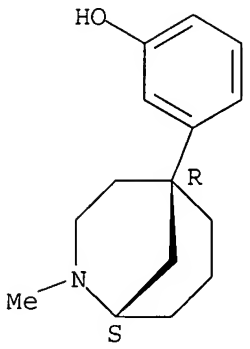
L6 ANSWER 56 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:85730 CAPLUS
DOCUMENT NUMBER: 76:85730
TITLE: Iminoethanophenanthridines by the Pictet-Spengler reaction
AUTHOR(S): Ong, Helen H.; May, Everette L.

CORPORATE SOURCE: Natl. Inst. Arthritis Metab. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Heterocyclic Chemistry (1971), 8(6), 1007-9
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Pictet-Spengler cyclization of 9-cis-amino-5-(m-methoxyphenyl)-2-methyl-2-azabicyclo[3.3.1]nonane (I) gave 2,3,4,4a,5,6-hexahydro-9-methoxy-3-methyl-1H-4,10b-propanobenzo[c][1,7]naphthyridine (II), derivs. of which were weakly analgesic. Thus, I was refluxed 4 hr in EtOH-HCHO-HCl to give 82% II. 2HCl, which was converted to the O-demethyl derivative (III) with HBr. III was treated with cyclopropylcarbonyl chloride-Et3N and the product reduced with LiAlH4 to give the 5-(cyclopropylmethyl) derivative (IV) of III. The hot-plate test showed that III and IV possessed .apprx.14% the analgesic activity of codeine.
IT **35190-80-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 35190-80-8 CAPLUS
CN Formamide, N-[5-(3-methoxyphenyl)-2-methyl-2-azabicyclo[3.3.1]non-9-yl]-, anti- (9CI) (CA INDEX NAME)

Relative stereochemistry.

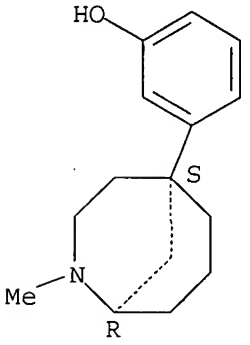



L6 ANSWER 57 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:487772 CAPLUS
DOCUMENT NUMBER: 73:87772
TITLE: Optical isomers of miscellaneous strong analgetics
AUTHOR(S): May, Everette L.; Takeda, Mikio
CORPORATE SOURCE: Nat. Inst. of Arthritis and Metab. Dis., Nat. Inst. of Health, Bethesda, MD, USA
SOURCE: Journal of Medicinal Chemistry (1970), 13(5), 805-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Optical isomers of α-5,9-diethyl-2'-methoxy- (Ia), α-2,5-dimethyl-9-ethyl-2'-hydroxy- (Id), and 2'-hydroxy-2-methyl-6,7-benzomorphans (Ic) and of 5-(m-hydroxyphenyl)-2-methylmorphan (II) have been prepared and compared with parent racemates in analgetic activity, physical dependence capacity, and antagonistic behavior. Racemate Ic, (+)-Ic, (-)-Ic and (-)-II, have morphine-like analgetic and nalorphine-like antagonistic action. Ia was prepared from Ib.
IT **27107-49-9P 27107-50-2P 28623-81-6P**
**28623-84-9P 31798-03-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)

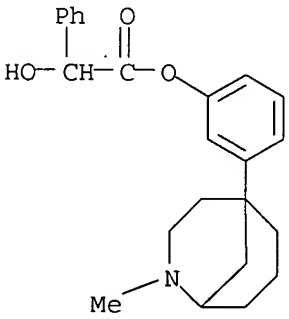



RN 28623-84-9 CAPLUS
CN Phenol, 3-[(1R,5S)-2-methyl-2-azabicyclo[3.3.1]non-5-yl]- (9CI) (CA INDEX NAME)

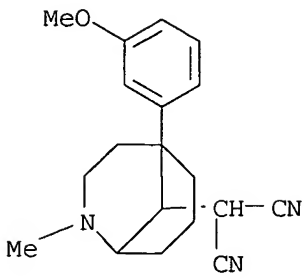
Absolute stereochemistry. Rotation (-).




RN 31798-03-5 CAPLUS
CN Mandelic acid, (+)-m-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)phenyl ester, D- (8CI) (CA INDEX NAME)




L6 ANSWER 58 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:122365 CAPLUS
DOCUMENT NUMBER: 53:122365
ORIGINAL REFERENCE NO.: 53:22043e-i
TITLE: Structures related to morphine. X. A position isomer of (±)-3-hydroxy-N-methylmorphinan (Racemorphan)
AUTHOR(S): May, Everette L.
CORPORATE SOURCE: Natl. Inst. of Arthritis and Metabolic Diseases,




● HCl

L6 ANSWER 59 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1958:11165 CAPLUS
DOCUMENT NUMBER: 52:11165
ORIGINAL REFERENCE NO.: 52:2032d-i
TITLE: Structures related to morphine. VI. N-Phenylethyl derivatives of some phenyl- and benzomorphans
AUTHOR(S): May, Everette L.
CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD
SOURCE: Journal of Organic Chemistry (1956), 21, 899-901
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

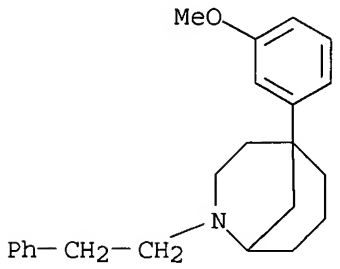
AB cf. C.A. 50, 15560h. N-Me derivs. were converted to N-phenylethyl analogs. These were shown two to three times less effective than the respective N-Me counterparts in producing analgesia in mice, contrary to results obtained with meperidine and race-morphan types. To 1.2 g. BrCN in 7 ml. dry CHCl3 was added 2.4 g. 5-(m-methoxyphenyl)-2-methylmorphan (I) in 10 ml. CHCl3 during 45 min. while stirring, refluxed 3 hrs., evaporated to dryness in vacuo, the residue dissolved in EtOH, refluxed briefly, evaporated to dryness, 10 ml. EtOAc added to recover 0.5 g. I.HBr, m. 158-62°. Filtrate freed from EtOAc in vacuo, the residue and 45 ml. 6% HCl refluxed overnight, cooled to 0°, basified with 10% KOH, the liberated oil dried in ether, 32% HBr-AcOH added, kept overnight at 0°, the semisolid washed with ether, and triturated with EtOAc containing a little acetone gave 1.3 g. 2-(m-methoxyphenyl)morphan-HBr (II), m. 127-30°, 67% yield (with 0.3 g. from filtrate), m. 129-31° (acetone-ether); picrate, yellow prisms, m. 162-5° (EtOH). Phenylacetyl chloride (1.0 ml.) added during 3-5 min. to a stirred mixture of 1.0 g. II, 1.5 g. $K_2CO_3$, 5 ml. $H_2O$, and 15 ml. MeOH, stirred 1 hr., diluted with 3 volume $H_2O$, extracted with ether, the extract washed with dilute HCl and dilute NaOH, dried, and evaporated to dryness gave 1.5 g. sirup, which in 20 ml. dry ether treated gradually with 20 ml. 1.4M ethereal $LiAlH_4$, refluxed overnight, treated carefully with 10-15 ml. $H_2O$, the ether decanted from residual hydroxides which were washed three times, combined ether portions dried, and acidified with 32% HBr-AcOH gave 1.1 g. 5-(m-methoxyphenyl)-2-(2-phenylethyl)morphan-HBr (III), leaflets, m. 209-11° (acetone). III (1.1 g.) refluxed in 7 ml. 48% HBr 30 min., evaporated to dryness, and the residue triturated with absolute EtOH containing a little acetone gave 0.8 g. 5-(m-hydroxyphenyl)-2-(2-phenylethyl)morphan-HBr, m. 274-7.5° (from MeOH). To 0.5 g. BrCN in 3 ml. CHCl3 was added 0.9 g. 5-phenyl-2-methyl-morphan in 5 ml. CHCl3 during 1 hr., refluxed 3 hrs., evaporated to dryness, dissolved in a little EtOH, refluxed

briefly, evaporated to dryness, and the residual sirup with 20 ml. 6% HCl refluxed overnight gave an almost clear solution which was shaken with ether, the aqueous layer basified with 10% NaOH, the oil in ether dried and brought to reaction with phenylacetyl chloride as described above. The resultant amide (1.3 g.) reduced with 15 ml. 1.4M ethereal $LiAlH_4$ gave 0.8 g. 5-phenyl-2-(2-phenylethyl)morphan-HBr, glittering plates, m. 264-7° (EtOH); picrate, yellow cubes, m. 184-6° (acetone-EtOH). By the same way, 1.6 g. 2,5-dimethyl-6,7-benzomorphan yielded 1.1 g. 5-methyl-2-(2-phenylethyl)-6,7-benzomorphan-HCl, m. 278-80° (decomposition) (absolute EtOH); picrate, m. 142-6° (EtOH).

IT **114279-13-9**, 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-phenethyl-, hydrobromide **114353-67-2**, 2-Azabicyclo[3.3.1]nonane, 5-(m-hydroxyphenyl)-2-phenethyl-, hydrobromide
(preparation of)

RN 114279-13-9 CAPLUS

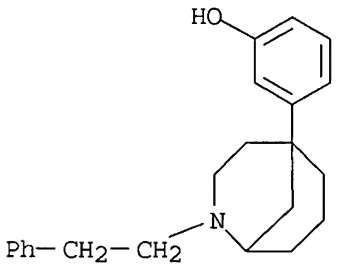
CN 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-phenethyl-, hydrobromide (6CI) (CA INDEX NAME)




● HBr

RN 114353-67-2 CAPLUS

CN Phenol, m-2-phenethyl-2-azabicyclo[3.3.1]non-5-yl-, hydrobromide (6CI) (CA INDEX NAME)




● HBr

L6 ANSWER 60 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1956:44580 CAPLUS

DOCUMENT NUMBER: 50:44580

ORIGINAL REFERENCE NO.: 50:8635d-i,8636a

TITLE: Structures related to morphine. IV. m-Substituted phenylcyclohexane derivatives

AUTHOR(S): May, Everette L.; Murphy, James G.

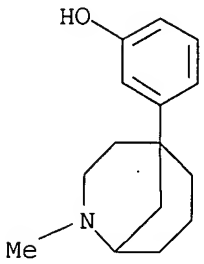
CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD
SOURCE: Journal of Organic Chemistry (1955), 20, 1197-1201
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:44580

AB cf. C.A. 50, 4165a. 1-(2-Dimethylaminoethyl)-1-(m-hydroxyphenyl)cyclohexane (I) and 5-(m-hydroxyphenyl)-2-methylmorphan (II) have been prepared to be tested for their analgesic activity. Stirring 14 g. 2-(m-methoxyphenyl)-1-nitro-4-cyclohexene in 105 cc. 95% EtOH 1 h. in a N atmospheric with 90 cc. alc. NaOEt (from 3 g. Na), then adding (40 min.) 240 cc. H2O, 180 cc. 95% EtOH, and 72 cc. concentrated HCl at -5° to 0° with stirring, stirring the mixture another hr. at 0° and 0.5 h. at 20°, pouring it into 1.2 l. ice-salt-H2O, extracting it quickly with Et2O, and evaporating the washed (saturated NaHCO3, H2O) Et2O extract in vacuo under N give 12.2 g. residue which is hydrogenated 40 min. in 25 cc. MeOH with 3 g. 5% Pd-BaSO4, giving 83% 2-(m-methoxyphenyl)cyclohexanone (III), b0.02 135-45° (air bath temperature), nD20 1.5497. Adding (5-10 min.) 8.8 g. III in 60 cc. C6H6 to 1.7 g. NaNH2 in 40 cc. refluxing C6H6, refluxing the solution 0.5-1 h., adding (30-45 min.) 4.8 g. CH2ClCH2NMe2 in 60 cc. C6H6, refluxing the mixture 20 h. with stirring, washing it with H2O, extracting it with dilute HCl, warming the acid extract slightly, washing it with Et2O, making it basic with NH4OH, extracting with Et2O, and treating the dried Et2O extract with dry HCl give 24% 2-(2-dimethylaminoethyl)-2-(m-methoxyphenyl) cyclohexanone-HCl (IV), prisms, m. 165.5-6.5°, and, from the mother liquors, 5.2 g. unchanged III. Heating 0.5 g. IV, 0.5 cc. 95% N2H4, 0.5 g. KOH, and 5 cc. triethylene glycol 6 h. at 180-210° and treating the reduction product with 32% HBr-AcOH give 90% 2-(2-dimethylaminoethyl)-1-(m-methoxyphenyl)cyclohexane-HBr (V), prisms, m. 167-8.5°. Refluxing 0.6 g. V 0.5 h. with 2.5 cc. 48% HBr and evaporating the solution in vacuo give 87% I.HBr, needles, m. 178-9° (HCl salt. needles, m. 191.5-3°). Treating 0.5 g. I.HBr in 0.5 cc. Ac2O and 1 cc. C5H5N 1 h. at 25°, diluting the mixture with Et2O, and keeping it overnight at 5° give 0.55 g. 1-(m-acetoxyphenyl)-1-(2-dimethylaminoethyl)cyclohexane-HBr, needles, m. 138-8.5°. Converting 12 g. IV into 12.4 g. HBr salt and treating the latter in 140 cc. refluxing AcOH with 6 g. Br in 50 cc. AcOH, diluting the mixture with 500 cc. Et2O, and keeping it overnight at -6° give 14.5 g. 6-Br derivative-HBr of IV, needles, m. 184-5°, which, treated 1-2 h. in 35 cc. H2O with 4 cc. concentrated NH4OH, gives 90% 5-(m-methoxyphenyl)-2-methyl-9-oxomorphan (VI) methobromide (VII), thick plates, m. 249-50° (decomposition). Dry distillation of 10.2 g. VII at 210-25°/0.5 mm. gives 89% VI.HCl, plates, m. 203-5° (decomposition). Heating 7.7 g. VI.HCl in 50 cc. triethylene glycol with 7 cc. 95% N2H4 and 7 g. KOH 5.5 h. at 175° and 0.5 h. at 190° gives 90% 5-(m-methoxyphenyl)-2-methylmorphan-HBr, oblong plates, m. 165-7°, which (7.7 g.), refluxed with 30 cc. 48% HBr, gives 80% II.HBr, m. 171-2° (free base, m. 156-7.5°; m-Ac derivative-HBr, 100%, small prisms, m. 162.5-3.5°). The results of the pharmacol tests of these compds. are given in a table.

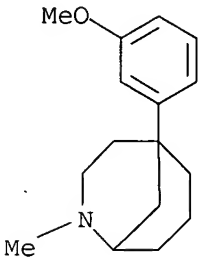
IT **27107-68-2**, 2-Azabicyclo[3.3.1]nonane, 5-(m-hydroxyphenyl)-2-methyl-
(and derivs.)

RN 27107-68-2 CAPLUS

CN Phenol, 3-(2-methyl-2-azabicyclo[3.3.1]non-5-yl)- (9CI) (CA INDEX NAME)




IT **53661-49-7**, 2-Azabicyclo[3.3.1]nonane, 5-(m-methoxyphenyl)-2-methyl-, hydrobromide
(preparation of)
RN 53661-49-7 CAPLUS
CN 2-Azabicyclo[3.3.1]nonane, 5-(3-methoxyphenyl)-2-methyl-, hydrobromide (9CI) (CA INDEX NAME)




● HBr

L6 ANSWER 61 OF 61 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1955:28257 CAPLUS
DOCUMENT NUMBER: 49:28257
ORIGINAL REFERENCE NO.: 49:5498d-i
TITLE: Structures related to morphine. II. An isomer of N-methylmorphinan
AUTHOR(S): May, Everette L.; Murphy, James G.
CORPORATE SOURCE: Natl. Inst. of Health, Bethesda, MD
SOURCE: Journal of Organic Chemistry (1954), 19, 618-22
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

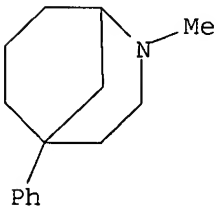
AB 1,2,3,9,10,10a-Hexahydro-11-methyl-1,4a(4H)-iminoethanophenanthrene (I), an isomer of N-methylmorphinan, has been synthesized from 2-(2-dimethylaminoethyl)-2-phenylcyclohexanone (II). II.HBr (0.005 mol) in 10 cc. refluxing AcOH is treated with 0.26 cc. Br in 10 cc. AcOH and the mixture refluxed 0.5 h., giving 88% 6-Br analog (III), tiny needles, m. 181-1.5°. Treating 34.6 g. III in 86 cc. H2O with 13 cc. concentrated NH4OH with ice-cooling gives 91% 9-keto-2-methyl-5-phenylmorphan (IV) methobromide (V), square plates, m. 238-8.5° (IV.HCl, prepared in 88% yield by dry distillation of V at 225-30°/0.1 mm. and treating the distillate in ether with HCl, needles, crystallizing with 0.5 mol H2O, m. 214-15°). Heating 2.2 g. IV.HCl with 0.8 cc. 95% N2H4, 1.6 g. KOH, and 8 cc. triethylene glycol 6 h. at 170-80%, diluting with H2O, extracting with ether, and treating the ether extract with HCl give 75% 2-methyl-5-

phenylmorphan.HCl, slender prisms, m. 239-40°. Refluxing IV (from 5.6 g. HCl salt), 1.4 g. $CH_2(CN)_2$, 0.4 g. $NH_4OAc$, 0.9 cc. AcOH, and 7 cc. $C_6H_6$ 1 h. with a $H_2O$ trap, extracting with ether, and treating the ether extract with alc. HCl gives 87% 9-dicyanomethylene-2-methyl-5-phenylmorphan (VI).HCl, slim prisms, m. 210-13° (decomposition). Hydrogenating 2 g. VI.HCl in 50 cc. MeOH with 0.1 g. $PtO_2$ 1.5 h. at 20°, evaporating the filtered solution in vacuo, refluxing the residue 6 h. with 20 cc. 20% HCl, evaporating again, and triturating the residue with $Me_2CO$ gives 46% 9-carbomethoxy-2-methyl-5-phenylmorphan (VII).HCl, minute prisms, m. 280° (decomposition). Heating 2.8 g. VII.HCl with 30 g. polyphosphoric acid 3 h. with stirring, diluting the mixture with ice-$H_2O$, pouring it into ice-$H_2O$ containing 45 g. KOH, and extracting with ether gives 93% 1,2,3,9,10,10a-hexahydro-9-oxo-11-methyl-1,4a-(4H)-iminoethanophenanthrene (VIII).HCl, blades containing 0.5 $H_2O$, m. 192-4° [picrate, yellow prisms, m. 220-2° (decomposition)]. Reduction of VIII with $N_2H_4$ gives 84% I.HCl, needles, m. 244-5.5° (decomposition) [picrate, yellow needles, m. 192-3° (decomposition)]. Heating the methiodide (m. about 320°) of I with 0.5 g. $Ag_2O$ and 5 cc. $H_2O$ 45 min. on a steam bath, evaporating the filtered solution in vacuo, and dry-distilling the residue at 120-30°/0.5 mm. give 0.25 g. distillate which, hydrogenated with $PtO_2$ 15-20 min. and treated with picric acid, gives 35% 4a-(2-dimethylaminoethyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (IX) picrate, yellow blades, m. 185-7°; it gives no m.p. depression when mixed with IX picrate obtained from n-methylmorphinan (cf. Grewe and Mondon, C.A. 43, 4279a). IX.HCl, square plates, m. 213-14°.

IT **74904-15-7**, 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride
(preparation of)

RN 74904-15-7 CAPLUS

CN 2-Azabicyclo[3.3.1]nonane, 2-methyl-5-phenyl-, hydrochloride (9CI) (CA INDEX NAME)




● HCl

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FILE 'REGISTRY' ENTERED AT 15:49:09 ON 24 JAN 2005

L1 STRUCTURE UPLOADED
L2 14 S L1
L3 STRUCTURE UPLOADED
L4 13 S L3
L5 408 S L3 FULL

FILE 'CAPLUS' ENTERED AT 15:53:54 ON 24 JAN 2005

L6 61 S L5

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=> d l3
L3 HAS NO ANSWERS
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

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## Inventor Name Search Result

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Last Name = COE
First Name = JOTHAM

| Application# | Patent# | Status | Date Filed | Title | Inventor Name 51 |
|---|---|---|---|---|---|
| 60497372 | Not Issued | 159 | 08/22/2003 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL | COE, JOTHAM WADSWORTH |
| 60497353 | Not Issued | 159 | 08/22/2003 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS | COE, JOTHAM W. |
| 60497350 | Not Issued | 159 | 08/22/2003 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL | COE, JOTHAM WADSWORTH |
| 60496803 | Not Issued | 018 | 08/21/2003 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF ADDICTION IN A MAMMAL | COE, JOTHAM WADSWORTH |
| 60488764 | Not Issued | 159 | 07/21/2003 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM W. |
| 60488760 | Not Issued | 159 | 07/21/2003 | HETEROARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM W. |
| 60469493 | Not Issued | 159 | 05/09/2003 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS | COE, JOTHAM W. |
| 60469429 | Not Issued | 159 | 05/09/2003 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE | COE, JOTHAM W. |

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| | | | | ADDICTION IN A MAMMAL | |
| 60462651 | Not Issued | 159 | 04/14/2003 | 4-PHENYL-PIPERIDINE COMPOUNDS AND THEIR USE AS MODULATORS OF OPIOID RECEPTORS | COE, JOTHAM W. |
| 60462629 | Not Issued | 159 | 04/14/2003 | 3-AZABICYCLO[3.2.1]OCTANE DERIVATIVES | COE, JOTHAM W. |
| 60462605 | Not Issued | 159 | 04/14/2003 | 2-AZABICYCLO[3.3.1]NONANE DERIVATIVES | COE, JOTHAM W. |
| 60416654 | Not Issued | 159 | 10/07/2002 | MODULAR UTILITIES MANIFOLD | COE, JOTHAM WADSWORTH |
| 60409694 | Not Issued | 159 | 09/10/2002 | DIAZABICYCLIC COMPOUNDS USEFUL IN THE TREATMENT OF CNS AND OTHER DISORDERS | COE, JOTHAM W. |
| 60303957 | Not Issued | 159 | 07/09/2001 | PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL | COE, JOTHAM W. |
| 60258736 | Not Issued | 159 | 12/29/2000 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS | COE, JOTHAM W. |
| 60221718 | Not Issued | 159 | 07/31/2000 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) | COE, JOTHAM W. |
| 60208856 | Not Issued | 159 | 06/02/2000 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS | COE, JOTHAM W |
| 60202799 | Not Issued | 159 | 05/09/2000 | PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF CONGNITIVE DYSFUNCTION IN A MAMMAL | COE, JOTHAM W. |
| 60195738 | Not Issued | 159 | 04/07/2000 | PHARMACEUTICAL COMPOSITION FOR TREATMENT OF ACUTE, CHRONIC PAIN AND/OR NEUROPATHIC PAIN AND MIGRAINES | COE, JOTHAM W. |
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| 10824037 | Not Issued | 020 | 04/14/2004 | 3-AZABICYCLO[3.2.1]OCTANE DERIVATIVES | COE, JOTHAM W. |
| 10823026 | Not Issued | 020 | 04/13/2004 | 4-PHENYL-PIPERIDINE COMPOUNDS AND THEIR USE AS MODULATORS OF OPIOID RECEPTORS | COE, JOTHAM W. |
| 10793112 | Not Issued | 030 | 03/04/2004 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE ADDICTION IN A MAMMAL | COE, JOTHAM W. |
| 10791984 | Not Issued | 030 | 03/03/2004 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS | COE, JOTHAM W. |
| 10783790 | Not Issued | 030 | 02/20/2004 | PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL | COE, JOTHAM W. |
| 10764167 | Not Issued | 092 | 01/23/2004 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM WADSWORTH |
| 10762730 | Not Issued | 030 | 01/22/2004 | 2-AZABICYCLO[3.3.1]NONANE DERIVATIVES | COE, JOTHAM W. |
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| 10681290 | Not Issued | 020 | 10/06/2003 | MODULAR UTILITIES MANIFOLD | COE, JOTHAM WADSWORTH |
| 10657738 | Not Issued | 030 | 09/08/2003 | DIAZABICYCLIC COMPOUNDS USEFUL IN THE TREATMENT OF CNS AND OTHER DISORDERS | COE, JOTHAM W. |
| 10366532 | Not Issued | 061 | 02/13/2003 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR TO FACILITATE OR PROMOTE WEIGHT LOSS | COE, JOTHAM WADSWORTH |
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| | | | | TREATMENT OF NICOTINE ADDICTION IN A MAMMAL | |
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| 10347955 | Not Issued | 161 | 01/21/2003 | PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF COGNITIVE DYSFUNCTION IN A MAMMAL | COE, JOTHAM WADSWORTH |
| 10336532 | Not Issued | 041 | 01/03/2003 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM WADSWORTH |
| 10336508 | Not Issued | 041 | 01/03/2003 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM WADSWORTH |
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| 10105605 | Not Issued | 161 | 03/25/2002 | PHARMACEUTICAL COMPOSITION AND METHOD OF MODULATING CHOLINERGIC FUNCTION IN A MAMMAL | COE, JOTHAM W. |
| 10075843 | Not Issued | 092 | 02/13/2002 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM WADSWORTH |
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| 10047850 | Not Issued | 161 | 10/23/2001 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF CNS AND OTHER DISORDERS | COE, JOTHAM WADSWORTH |
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| 09850042 | Not Issued | 161 | 05/07/2001 | PHARMACEUTICAL COMPOSITION FOR THE TREATMENT OF OBESITY OR | COE, JOTHAM WADSWORTH |

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| | | | | TO FACILITATE OR PROMOTE WEIGHT LOSS | |
| 09760966 | Not Issued | 161 | 01/16/2001 | PHARMACEUTICAL COMPOSITION AND METHOD OF TREATMENT OF DISEASES OF COGNITIVE DYSFUNCTION IN A MAMMAL | COE, JOTHAM WADSWORTH |
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| 09697749 | Not Issued | 161 | 10/26/2000 | PHARMACEUTICAL COMPOSITION FOR THE PREVENTION AND TREATMENT OF NICOTINE ADDICTION IN A MAMMAL | COE, JOTHAM W. |
| 09582513 | 6462035 | 150 | 08/07/2000 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM WADSWORTH |
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| 09514002 | 6605610 | 150 | 02/25/2000 | ARYL FUSED AZAPOLYCYCLIC COMPOUNDS | COE, JOTHAM W. |

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